CASE REPORT

Buschke–Löwenstein tumor (giant condyloma acuminatum) successfully treated by topical photodynamic therapy: a case report

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A B S T R A C T

Giant condyloma acuminatum (Buschke–Löwenstein tumor) is a rare sexually transmitted disease caused by human papilloma virus infection in the anogenital area. It is characterized by rapid growth, large size, local destruction, lack of spontaneous resolution, poor response to conservative therapy (e.g., cryotherapy), and a high recurrence rate. Treatment of such tumors remains challenging. We report the case of a 56-year-old Taiwanese man with a 9-month history of the Buschke–Löwenstein tumor with rectal invasion, treated by topical photodynamic therapy. We applied 16% methyl aminolevulinate for 3 hours and irradiated the tumor with 630-nm light at a dose of 37 J/cm² every 4–6 weeks. After three therapy sessions, the tumor disappeared without any scar or anal function impairment. Remote lesions that had been identified in the rectum also disappeared. Pain was the main side effect during treatment, but it was controlled by oral gabapentin. No recurrence was noted at 12-month follow-up or to date.

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Introduction

Giant condyloma acuminatum (GCA), also known as the Buschke–Löwenstein tumor, is a rare sexually transmitted disease associated with human papilloma virus (HPV) infection, mostly Type 6 or 11. The tumor is typically located on the glans penis. However, GCA may be discovered on any anogenital mucosal surface, including the vulva, vagina, anus, rectum, and scrotum.1,2 These tumors are characterized by rapid growth, large size, local invasion, lack of spontaneous resolution, poor response to conservative therapy (e.g., cryotherapy), and a high recurrence rate.3,4 The risk of neoplastic transformation into squamous cell carcinoma has been reported.2,5 In 1925, Buschke and Löwenstein reported a GCA as a benign carcinoma-like condyloma acuminatum. In 1965, the first case of anorectal GCA was reported by Dawson et al.2

Several authors have suggested that GCA is a type of low-grade squamous cell carcinoma, but others disagree. The controversy centers on the clinically malignant growth pattern that, nonetheless, shows benign histological features. The characteristic histological feature is a well-differentiated hyperplastic epithelium with minimal atypia. Hyperkeratosis and parakeratosis with a prominent granular layer and koilocytic changes have also been noted. An endophytic growth pattern with increased mitotic activity in the basal layer is evident, but this excludes the basement membrane and neural or vascular invasion.1,3,5 Traditional therapy includes surgical excision, CO2 laser treatment, fulguration, chemotherapy, radiotherapy, and immunotherapy.

We report the case of a patient with GCA who was treated with topical photodynamic therapy. The therapeutic response was complete and without recurrence.

Case presentation

A 56-year-old Taiwanese man was admitted to the dermatology inpatient ward at Kaohsiung Medical University Hospital. A mass had been present over the anal region for the past 9 months (Figure 1A), and the patient reported associated pain and changes in bowel habits; he also had difficulty walking and defecating.

Dermatologic examination revealed a flesh-colored, cauliflower-like tumor mass involving the anal area, and some verrucous papules scattered across the buttocks and scrotum. The tumor measured 10 × 5 cm².

The patient reported that initially the lesions had been scattered around the anal region but had enlarged rapidly within 5 months. He visited his local doctors and was treated with liquid nitrogen and imiquimod for 4 months. However, the mass was still growing and he sought our help. Laboratory examinations were conducted.
to check the patient’s immune system and status for sexual diseases other than HPV, including syphilis and HIV. The results were unremarkable, and the patient’s renal and hepatic functions were also within the reference range. No evidence of diabetes mellitus was found. Although rectoscopy was challenging because of the obstruction caused by the tumor, numerous verrucous papules were palpable by digital examination.

Skin biopsy revealed severe hyperkeratosis, papillomatosis, and parakeratosis with koilocytic changes. Increased mitotic activity was observed, but without any malignant changes. In addition to exophytic growth, endophytic invasion was apparent, with an intact basement membrane. Mild lymphocyte infiltration and blood vessel proliferation were apparent over the upper dermis (Figure 2).

To avoid anal function impairment, topical photodynamic therapy was performed. After gentle abrasion of the keratosis, we applied 16% methyl aminolevulinate (Metvix; Galderma, Watford, Herts, UK) to the lesions and surrounding 5–10 mm of perilesional normal skin by occlusion with a polyvinyl chloride dressing. After 3 hours, the dressing was removed and the lesion was irradiated using a light-emitting diode (LED) (Aktilite CL16; Galderma). The peak emission of 630 nm was used and the total dose was 37 J/cm². After this single treatment session, a month was allowed to elapse.

At the second consultation (1 month after the first treatment), the tumor size was found to be reduced and the patient received a second application of photodynamic therapy (Figure 1B). Another month elapsed, and we then applied Metvix and examined the lesion. We used the FotoFinder dermoscope dynamic (FotoFinder Systems GmbH, Bad Birnbach, Germany; www.fotofinder-systems.com/dermoscope), which can detect the red fluorescence of protoporphyrin IX accumulation in an infected area after the uptake of aminolevulinate.

Several residual lesions showing red fluorescence were detected over the anal region (Figure 3). The patient thus received a third session of photodynamic therapy (Figure 1C). Digital examination showed that the rectal lesions had disappeared.

The patient complained of tingling pain during the first session of photodynamic therapy. Hence, we gave him oral gabapentin (300 mg twice daily) during the second and third sessions, and this successfully controlled his pain.

Discussion

Treatment of GCA can be classified into three types: topical therapy (e.g., using podophyllin, fluorouracil, or radiotherapy), tumor removal (e.g., by cryotherapy using liquid nitrogen, CO₂ laser therapy, electrocautery, or surgical excision), and immunotherapy (e.g., using imiquimod). However, no gold standard currently exists for treating this rare disease, and the choice of treatment depends largely on the physician’s experience and skills.

The existing therapies frequently provide unsatisfactory results, with a slow response and high recurrence rate. A Medline search of the English literature from 1955 to 2006 was conducted using the following terms: “perianal giant condyloma acuminatum,” “Buschke–Löwenstein tumor,” and “treatment of giant condyloma acuminatum of the perianal region.” Their results showed that patients who accepted surgical excision, either with or without other therapy, experienced a recurrence rate as high as 50–66%. Alternative therapies are applied in cases of disease recurrence, but their effectiveness has not been well documented. Surgical removal and skin graft repair are complex procedures, and no standard surgery for GCA has been established to date. Patients must endure the risk of anesthesia and must be able to tolerate discomfort after the operation. The preservation of the anal sphincter function is an important issue during surgery. In our patient, rectal invasion wasuntreatable by any previously documented method.

The use of photodynamic therapy as an antiviral treatment may date back as early as the 1930s, when Schultz and Krueger discovered the antiviral action of photosensitizers. Topical photodynamic therapy using aminolevulinic acid hydrochloride (ALA) is a relatively new technique that was widely discussed in the 1990s. Methyl aminolevulinate is a prodrug that is transformed to endogenous protoporphyrin IX. It shows two individual absorption peaks at approximately 400 and 630 nm. We used 400 nm to detect...
fluorescent images using PhotoFinder and 630 nm to provide the LED light therapy. The ALA is selectively absorbed by rapidly proliferating cells, resulting in a high concentration of protoporphyrin IX production in the lesion. The protoporphyrin IX is activated by red light, resulting in the formation of reactive oxygen species. This process leads to a photochemical reaction and phototoxicity to the proliferating cells, resulting in cell death.3,7,8

Photodynamic therapy triggers an intense activation of inflammatory cells and promotes local immunity. Patients have been shown to exhibit a marked clinical and histological inflammatory response after photodynamic therapy. Evidence suggests that inflammatory cells participate in photodynamic therapy-induced tumor regression. At the biomolecular level, photodynamic therapy may induce several proinflammatory cytokines to promote an inflammatory response.3,7,8 These cytokines may help eliminate infected cells and reduce the risk of disease recurrence. Immunohistochemical studies performed on serial biopsies have shown that immunoreactivity over the lesion is a dynamic process and that T-lymphocytes increase within the first month after photodynamic therapy. Several patients in these studies demonstrated almost complete clearance. This finding suggests that the crucial therapeutic effect of photodynamic therapy is the induction of specific immunity.3,7,8

Patients frequently report that photodynamic therapy illumination is accompanied by a burning sensation and stinging pain; these appear to be the most common complications. The mechanism of this pain is not fully understood, but nerve stimulation and tissue injury might be involved. According to one hypothesis, gamma-aminobutyric acid (GABA) receptors in the peripheral nerve endings might be responsible for transporting ALA.9

![Figure 2](image1.png)

Figure 2 Histopathology of Buschke–Löwenstein tumor (hematoxylin and eosin stain) showed (A) marked hyperkeratosis, papillomatosis, and acanthosis (200×), (B) conspicuous koliocytes in epidermis (200×), (C) numerous mitotic cells in basal and peribasal layers (400×), and (D) intact basement membrane without squamous cell carcinoma-like malignant transformation or invasiveness (100×).

![Figure 3](image2.png)

Figure 3 Red fluorescence image detected by FotoFinder dermoscope dynamic. (A) Bright field. It was difficult to detect the infected lesions. (B) We applied 16% methyl aminolevulinate for 3 hours and examined the anal region by the FotoFinder dermoscope dynamic. Several residual lesions showing red fluorescence were detected over the anal region.
Therefore, we used gabapentin to block the GABA receptors. This proved to be an extremely beneficial method of pain control during photodynamic therapy for our patient.

The rapid growth of condyloma usually occurs in immunocompromised patients. Our patient did not test positive for HIV infection (which was confirmed by a second test after an interval of 18 months), but he might have sustained a wound or defect in the innate immunity of the mucosa. The active viral replication of a giant condyloma occurs on the tumor surface, where ALA penetration and light illumination are achieved relatively easily. In addition to the direct cell death and acute inflammation induced by photodynamic therapy, a delayed antiviral immune response is triggered, which can break down remote lesions in the rectum and prevent their recurrence.3,7,8

Compared with the three conventional therapies for GCA, photodynamic therapy offers the following advantages: avoidance of surgical complications and systemic side effects, preservation of anal function and intact appearance, elimination of virus-infected cells, and a reduced chance of disease recurrence. We therefore conclude that photodynamic therapy provides a promising alternative for treating cases of GCA.

References