

Treatment of Bowen's Disease on the Penis with Low Concentration of a Standard Mixture of Solasodine Glycosides and Liquid Nitrogen

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The most common form of penile cancer is squamous cell carcinoma (SCC). Due to the high risk for lymph node metastases, penile SCC is usually treated aggressively with Mohs micrographic surgery, excision with wide margins, or penectomy. These procedures have the potential for disfigurement and dysfunction of male genitalia, with associated psychological distress. Therefore, when treating superficial SCC (Bowen's disease) of the penis, a more conservative approach is feasible and often desired by the patient. Nonsurgical treatment options include topical 5-fluorouracil, imiquimod, neodymium-doped yttrium aluminium garnet (Nd:YAG) or carbon dioxide (CO₂) laser, and localized radiation. Here, we report a case of Bowen's disease of the penis successfully treated using a combination approach with a standard mixture of solasodine glycosides (BEC5) and supplemental liquid nitrogen used only on thickened, verrucous genital warts that were also present on the penis.

Case Report

A 52-year-old recently circumcised man with a history of long-standing verrucous condylomata acuminata presented with an erythematous macule on his penis. He reported first noticing the lesion after his circumcision and denied any symptoms, such as itching, bleeding or pain; he said that this

lesion did not resemble his typical genital warts. Biopsy showed Bowen's disease (SCC in situ) (Figure 1). Two courses of topical 5% imiquimod cream (Aldara, Graceway Pharmaceuticals, Bristol, TN) were attempted over 2 years; response was initially satisfactory, with clinical resolution, but the lesion returned 1 year after he finished the second course of imiquimod. At that time, a second biopsy specimen confirmed SCC in situ confined to the epidermis. Histologically, there was an atypical proliferation of keratinizing epithelial cells extending through the full thickness of the epidermis, with adnexal involvement. Nuclear pleomorphism was moderate to marked, and mitotic figures were numerous. Dermal invasion was not present.

The patient refused treatment with Mohs micrographic surgery because of the potential, yet necessary, disfigurement and loss of function. After a web-based literature search, he requested treatment with a low concentration of BEC5 (Dr. Cham's Curaderm, Curaderm Global Ltd, Queensland, Australia). The standard BEC5 mixture contains 0.005% BEC (33% solamargine, 33% solasonine, and 34% di- and monoglycosides), 10% salicylic acid, 5% urea, 0.1% melaleuca oil, and 0.05% linolenic acid in an oil-in-water cetomacrogol-based cream. The patient voiced an understanding that this treatment had not been used for his specific condition and that it might not

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Figure 1. Bowen's disease on the penis.

provide a cure, but he still desired to proceed with the treatment. The lesion was treated with topical BEC5 cream applied twice daily under occlusion. The patient was instructed to clean the area with a mild antiseptic, apply a thick coat of BEC5 cream, and cover the medicated area with a hypoallergenic micropore paper tape dressing. Liquid nitrogen was used monthly only to reduce focal thickened verrucous lesions (condylomata acuminata).

Two months after starting BEC5 therapy, the lesion showed minimal response (Figure 2). Marked clinical improvement was observed after 4 months, and by his 9-month follow-up visit, even greater regression of the erythematous macule was noted (Figure 3). At 10 months, the lesion was no longer clinically apparent, and the BEC5 treatment was stopped; this was in accordance with previous literature reports that the endpoint of therapy should correspond with re-epithelialization of treated skin.^{1,2} No clinical recurrence was observed over 2 years after completion of treatment with BEC5 (Figure 4). Side effects during the treatment were limited to transient local irritation and ulceration; these resolved when treatment was discontinued.

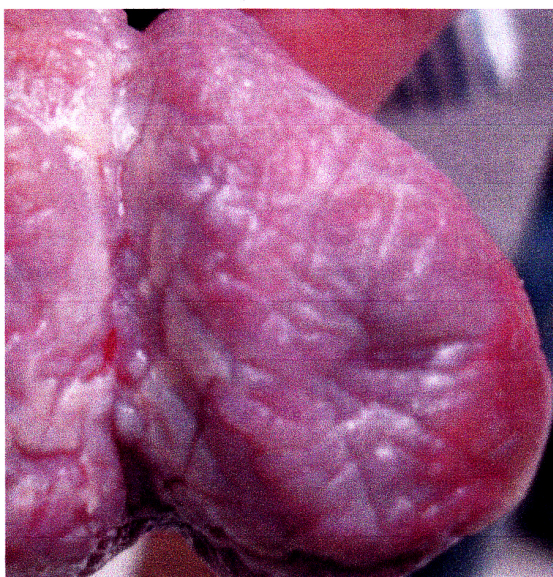


Figure 2. Two months after starting treatment with a standard mixture of solasodine glycosides and liquid nitrogen.

Discussion

Penile cancer accounts for less than 1% of male cancers in Western countries, although it can

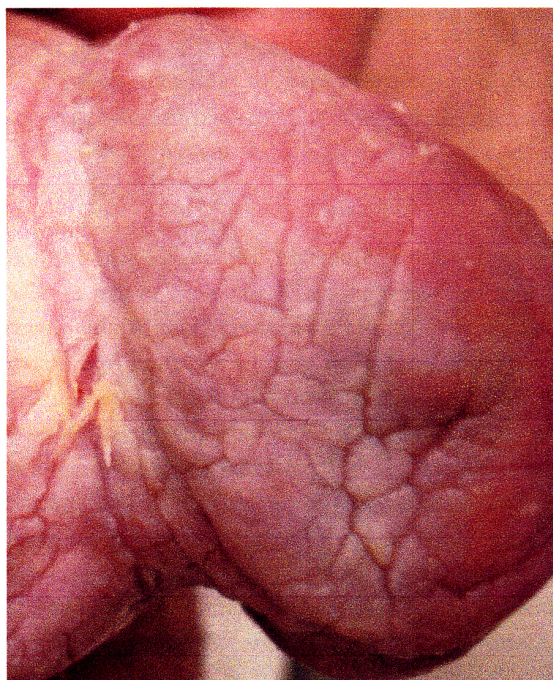


Figure 3. Nine months after starting treatment with a standard mixture of solasodine glycosides and liquid nitrogen.



Figure 4. Two-year follow-up after completion of treatment with a standard mixture of solasodine glycosides and liquid nitrogen.

account for up to 20% in underdeveloped countries³⁻⁵; 90% to 95% of penile malignancies are SCCs.^{3,4} They most commonly occur in older men (50-80) and are much more prevalent in men who were not circumcised early in life.³⁻⁶ Additional risk factors include poor hygiene, smoking, and phimosis. SCC in situ of the penis includes erythroplasia of Queyrat and Bowen's disease, which can progress to invasive SCC with the potential for metastases to the local lymph nodes and possibly to more-distant regions of the body.^{7,8} Human papilloma virus infection has been reported in 15% to 80% of men with penile cancer, but no definitive causal relationship has been established.^{4,6,8}

Mohs surgery is a safe and effective treatment option³ that allows for the best possible cure rate, maximal tissue sparing, and complete margin control; it may be considered the surgical treatment of choice for Bowen's disease of the penis. With invasive SCC, local lymphatic metastases are the rule, not the exception, and treatment must be more extensive, including partial or total penectomy, sentinel lymph node biopsy, and lymphadenectomy as indicated.^{3,4}

When treating SCC of the penis that is histologically proven to be confined within the epidermis, several nonsurgical treatment options exist, with varying degrees of efficacy and recurrence risk. These include 5-fluorouracil, imiquimod, laser treatment with the Nd:YAG (1,064-nm) or CO₂ laser (10,600-nm), and radiation.⁹⁻¹² Recently, a topical formulation of three isolated solasodine glycosides: 33% solamar-gine, 33% solasonine, and 34% di- and monoglycosides (BEC5) was introduced for the treatment of in situ and malignant skin lesions.^{1,2}

The main component of BEC5 is a specially purified extract from an Australian plant (*Solanum sodom-aeum*) known commonly as the Devil's Apple and is also found in eggplant. It is a relatively new product for the nonsurgical treatment of skin cancer. An Australian biochemist introduced it to the medical world after he heard a folk tale about a cow that cured its own tumor by consistently rubbing its face in a patch of these weeds. The active ingredients of BEC5 are rhamnose sugar moieties, which do not occur naturally within mammalian species. Healthy mammalian cells do not possess receptors for these sugar moieties, but cancer cells do.^{13,14,16,17} After BEC5 molecules bind to these cancer-specific receptors, they are internalized and lead to cell death in a process that involves lysosomal destruction and apoptosis.^{1,13,14,16,17}

As far as we know, BEC5 has not been used to treat SCC in situ of the penis. Previous studies of topical formulations have reported its use only on the face, trunk, and limbs.^{1,15} During treatment, patients develop areas of inflammation in and around the tumor, which may necrose,^{1,2} leading to ulceration and healing by reepithelialization.^{1,15} The endpoint of therapy coincides with regrowth of skin at the treatment site.^{1,2} Although these side effects may be bothersome to many people, our patient consistently applied the BEC5 cream and adhered to treatment recommendations because he preferred any side effects of the cream to a surgical alternative. He did not consider taking "holidays" and did not complain much about pain and inflammation.

A clinical study evaluated the efficacy of BEC5 (Curaderm) at a 0.005% concentration for treating SCC, basal cell carcinoma (BCC), and keratoses on the face, extremities, and trunks.¹ Complete histologic and clinical regression was found in all lesions (124 lesions in total), with no clinical recurrences 1 to 3 years after treatment.¹ Reported side effects were itching, burning, redness, and swelling of and around the treated regions.¹ A previous study with a higher concentration of BEC (10%) found complete regression of tumors in 83% of patients with BCC and SCC.² A separate group evaluated a different formula (Zycure) of 0.005% solasodine glycosides (mostly solasonine and solamargine) for the treatment of BCC and found a 66% response rate, with 78% of these patients returning for follow-up without recurrence.¹⁵ Curaderm and Zycure proved more effective than placebo.^{1,15}

Our patient experienced a typical response to BEC5, including inflammation and necrosis followed by ulceration and reepithelialization of the treated skin. There was complete clinical regression of his tumor after combination treatment with BEC5 and liquid nitrogen for adjacent condyloma. This combination approach consisting of generalized application of BEC5 augmented by localized use of liquid nitrogen for verrucous lesions was advantageous in that it limited the pain and risk of scarring from excessive use of liquid nitrogen alone or surgery.

We report the successful treatment of Bowen's disease of the penis with BEC5. This tissue-sparing technique preserves functionality and may be a promising alternative to other more-destructive treatment options for Bowen's disease of the penis. Further long-term, prospective studies with larger patient populations are recommended to further assess this treatment of SCC of the penis.

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