

**Case Report**

Giant Condyloma Acuminatum Covering the Vulva, Edges of the Labia Minora and Majora and Anus was Successfully Eliminated with MVA E2 Recombinant Virus Therapeutic Vaccination

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Abstract

In this report, we present a case of a large condylomata acuminata lesion in an adolescent 14-year-old female. The condyloma was injected directly with 10^7 MVA E2 virus particles once a week for an 8-week period. The lesion was monitored by colposcopy every week with the application of acetic acid. The patient was positive for serum antibodies against Human Papillomavirus 11 (HPV 11). Complete regression of the lesion was observed after treatment. No apparent side effects or recurrences were observed at one year of follow-up. This case report suggests that therapeutic vaccination with MVA E2 is an excellent option to achieve regression of anogenital papilloma lesions.

Keywords: Condyloma; MVA Strain; Papillomavirus; Vaccinia Virus

Introduction

Human papillomavirus produces benign lesions, named papillomas [1,2]. These small, wart-like neoplasias are present in the anogenital mucosa and skin and in very rare cases invade the vulva and vagina [3,4]. However, in some cases, papillomas can become large condyloma lesions, destroying the epithelium. Additionally, vulvar HPV infection can lead to the development of benign tumors (condylomata acuminata) [5]. Probably because of the weak immune response against the papillomavirus-infected cells. The most common viruses found in this type of lesion are HPV 6 and HPV 11 [1]. And HPV 11 is found in one-fourth of genital warts. [5,6] Furthermore, the rate at which lesions grow may depend on the genetic constitution of the patients as well as the possible HPV variant involved. Standard procedures, such as

cryotherapy, trichloroacetic acid, and laser or surgical removal, provide very good treatment for these lesions [7]. Nonetheless, recurrences and reinfections occur because these procedures are not able to eliminate the HPV [8,9]. In addition, it is well known that HPV can inhibit the recognition of malignant cells by the immune system, leading to the development of lesions [10-16]. Recently, we described the therapeutic approach involving the recombinant vaccinia virus strain MVA E2 to treat many types of lesions generated by papillomaviruses [17-23]. Here, we present one of the few cases of a giant condyloma covering the anogenital tract and its complete elimination by treatment with the MVA E2 therapeutic vaccine.

Case Report

A 14-year-old female was admitted to the Medical Center-San Patricio with a Giant Condyloma Acuminatum (GCA) lesion in the vulva and perianal area. According to the clinical history, the

patient had only one sexual partner. Macroscopic examination of the lesion revealed a length of 8 cm, width of 5 cm and thickness of 0.5 mm (Figure 1). The lesion grew over approximately 6 months and did not interfere with defecation; no bleeding was observed. A biopsy sample was not taken because of the high degree of pain presented by the patient. The presence of high levels of antibodies against HPV 11 was detected in her serum [24]. The patient did not present other infectious diseases that may have contributed to the generation of the giant condyloma. The lesion was treated by injecting 10^7 virus particles of the MVA E2 therapeutic vaccine inside the lesion and in the basal epithelium of the lesion once a week for an 8-week period. One month later, tiny spots of the remaining condyloma were eliminated with the application of Trichloro Acetic Acid (TCA).



Figure 1: Photographs of the giant condyloma acuminatum lesion from a young female patient. Tissue after 0, 4, 6, and 8 weeks of MVA E2 treatment is shown. The patient was completely free of lesions after treatment, and no regression was observed after one year of follow-up.

Lesion reduction was monitored weekly and no recurrence was observed during the one-year follow-up. Adverse side effects did not occur in this patient. Additionally, colposcopy examination using acetic acid showed no-aceto white spots in the lesion area. Overall, MVA E2 is an excellent immunotherapy tool for treating large papillomavirus lesions.

Discussion

Giant condyloma acuminatum is a rare lesion found in the anogenital area [4,25,26]. These lesions are mostly related to low-risk HPV infections, and do not represent a risk of malignant transformation. Nevertheless, these lesions can be found in immunosuppressed individuals as well as in HIV-positive patients [4]. In some cases, vulvar cancer, which is very rare, occurs and

may be confused with genital condylomata, [27] which constitutes a good reason to examine in detail the type of lesion as well as the HPV genotype present in these lesions.

Although the first choice for treatment of GCA is a wide surgical excision, a high recurrence rate (30-70%) has been reported, [28] and this procedure destroys many epithelial cells. Preserving the normal functionality as well as the aesthetics of this region is essential.

When surgery is contraindicated, treatments such as chemotherapy (podophyllin, 5 fluorouracil, bleomycin, and methotrexate), radiotherapy, laser therapy, cryosurgery and electrocoagulation have been applied [29]. Despite being good treatments, there are disadvantages with these methods, such as

adverse side effects, with recurrence in most cases. The appearance of new lesions after performing these conventional treatments is likely due to the lack of antibody production as well as the generation of cytotoxic cells, which are the main immunological protection of the body.

The development of anticancer vaccines as immunotherapy has been shown to be a promising alternative to treat and eradicate virus-induced tumors generated by papillomaviruses [21,30-32]. The recombinant MVA E2 virus vaccine is a Modified Vaccinia Virus Ankara (MVA) containing the bovine papillomavirus E2 gene [23]. MVA E2 is a therapeutic vaccine that can induce a strong immune response against HP-transformed cells. MVA E2 induces antitumor antibodies that exert antibody-dependent cell-mediated cytotoxicity [21]. Additionally, MVA E2 causes formation of specific cytotoxic cells against tumor cells [19,20,22] which is the main mechanism of this recombinant virus for the lesion regression.

In contrast, to preventive vaccines, only the humoral response is detected, mainly via production of antibodies against HPV-virus particles.

Here, we show that MVA E2 is capable of completely eliminating a large condylomata lesion. Thus, local application of MVA E2 is an efficient approach to stimulating the eradication of HPV lesions. In addition, no apparent side effects were recorded. This result agrees with our previous work in which injection of the MVA E2 virus into the lesions was able to stimulate complete regression as well as the formation of specific cytotoxic cells against papilloma-transformed cells. MVA E2 can also induce a long-lasting immunity that prevents lesion recurrence in most patients [19,20,22].

In several countries, immunization of females younger than 26 years of age with the quadrivalent HPV vaccine (Gardasil) reportedly reduces the incidence of condyloma acuminata [33]. This may be because an increased amount of specific antibodies against HPV can prevent the papillomavirus from infecting epithelial cells in some patients. Regardless, once HPV enters cells, with eventual transformation, it becomes very difficult to eliminate lesions with prophylactic vaccines [34]. One report found successful elimination of GCA with imiquimod, with no recurrences after 3 years of follow-up [3]. However, the treatment with imiquimod has important inflammatory side effects, including itching, erythema, burning, irritation, tenderness, ulceration, and pain; thus, its use in mucosal tissue is limited [35]. Moreover, the health conditions as well as the immunological status of the patient should be considered before implementing this procedure.

Another study showed the elimination of giant condyloma acuminata via an innovative surgical method, in which the lesion was excised by clamping and cutting the pedicles without damage

to the perineal and perianal areas, resulting in a low recurrence [36]. However, this method is difficult to perform, and the elimination of HPV using this procedure is very rare. Thus, the MVA E2 therapeutic vaccine is probably the best tool for the treatment of many different types of HPV-lesions and may be a promising therapy to eradicate cervical cancer worldwide.

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Disclosure Statement

The authors declare that no competing financial interests exist and that there are no conflicts of interest between the authors.

Informed Consent

The patient (Parents) provided a written informed consent, and the study design was approved by the appropriate ethics board.

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