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Case Report

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Treatment of Condyloma Acuminata in the Penis with Subcutaneus Interferon Alfa 2b: Report of a Case

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Abstract

Condyloma acuminata, also known as genital warts, are lesions caused by the human papillomavirus (HPV). Genotypes 6 and 11 are responsible for more than 90% of cases. They represent one of the most common sexually transmitted diseases. The usual locations are external genitalia (penis, vulva, perineum, and perianal skin), cervix, vagina, urethra, and anus. Diagnosis is generally clinical. Factors to consider in selecting treatment include the size, number, and morphology of the lesions, the affected anatomical site, patient preference, cost, convenience, side effects, and the professional's experience. Many patients require more than one treatment. Interferon (IFN) is a group of glycoproteins that are naturally produced and have antiviral, antiproliferative, and immunomodulatory properties. When administered subcutaneously, it is an effective, non-invasive therapeutic option with few side effects for multiple condyloma acuminata. We present a patient with multiple condyloma acuminata with a very satisfactory response to subcutaneous IFN alpha 2b.

Keywords: Condyloma acuminata, Human papillomavirus, Genital warts, Interferon alpha 2b.

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Introduction

HPV infection is considered the most common sexually transmitted infection [1]. It particularly affects young women and men, and its incidence is directly related to sexual activity [1, 2]. There are more than 200 HPV genotypes, which are clinically grouped into low- and high-risk oncogenic types. The former (HPV 6 and 11) are responsible for anogenital warts, very common benign lesions. The high-risk oncogenic types (HPV 16 and 18) cause dysplastic lesions considered direct precursors of many neoplasms, especially of the cervix, anus, and oropharynx [2, 3]. The clinical expression of genital HPV infection is variable, ranging from asymptomatic states with spontaneous resolution to cancerous processes [4].

Among the common clinical manifestations are condylomata acuminata, also called genital or anogenital warts. These are benign, proliferative lesions, usually multiple, pink or grayish white in color, sometimes hyperpigmented, with filiform or papillomatous projections on their surface. They are generally exophytic lesions, sessile or pedunculated, but can be flattened. They are usually located in the anogenital region, in areas of greater trauma during sexual intercourse [4, 5].

The diagnosis of the infection is clinical and is confirmed by molecular techniques based on the detection of viral DNA and mRNA of oncogenic proteins. Histopathological examination reveals the cellular alteration caused by the infection (koilocytosis) [6]. For the treatment of anogenital warts, each case must be evaluated individually, taking into account various factors, such as the psychological impact, the extent and type of lesions, the duration of the condition, the patient's immune status, the cost, and even the physician's experience. Treatment does not eradicate the HPV infection but rather eliminates the warts and improves symptoms when present [6, 7]. Based on their mechanism of action, treatments are divided into three types:

- Physical: radiofrequency-loop electrosurgical excision procedure, surgery, laser, electrocoagulation, and cryosurgery.
- Chemical: Trichloroacetic acid, podophyllin, and podophyllotoxin.
- Immunomodulators: IFN, imiquimod, and 5-fluorouracil [8].

IFN is a group of naturally occurring glycoproteins with antiviral, antiproliferative, and immunomodulatory properties. Subcutaneous administration is an effective, non-invasive therapeutic option for multiple condylomata acuminata with few adverse effects [9, 10]. We present the case of a patient with multiple condylomata acuminata who had a highly satisfactory response to subcutaneous IFN alpha-2b treatment.

Case Report

A 21-year-old man with no known medical history presented

with penile warts of four months' duration (Figure 1). The warts were asymptomatic and had been progressively increasing in number and size. He had undergone topical treatment with 50% trichloroacetic acid twice without improvement. Laboratory tests were within normal limits, and serological tests (Human immunodeficiency virus, hepatitis B virus, hepatitis C virus, quantitative venereal disease research laboratory) were non-reactive. The histopathological study of one of the lesions revealed hyperkeratosis, acanthosis, papillomatosis, koilocytosis, and intercellular edema (Figure 2 and figure 3). The typing was conclusive for HPV 11. Final diagnosis: multiple condylomata acuminata due to HPV 11.

Due to the location, size, and number of lesions, treatment with subcutaneous IFN alpha 2b at a dose of 1.5 million international unit (IU) per week for 6 weeks was indicated. Due to lack of response, the dose was doubled, resulting in an additional 6 weeks of subcutaneous IFN alpha 2b at 3 million IU, for a total of 12 weeks of treatment.

Figure 1: Multiple warts that affect the entire penis, predominantly the glans and balanopreputial sulcus, and extend to the pubis.

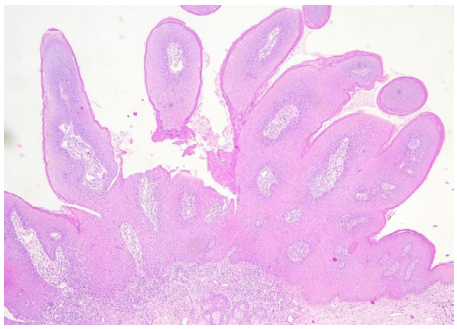

Figure 2: HyE 4X. Acanthosis and papillomatosis.

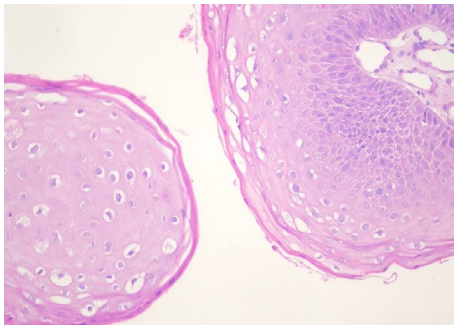

Figure 3: Hematoxylin and Eosin 40X. Hyperkeratosis, acanthosis, and koilocytosis.

The patient progressed satisfactorily, with resolution of almost all lesions (Figure 4). Topical treatment with podophyllotoxin 0.5% gel was then prescribed 3 days a week for one month, and complete disappearance of the warts was achieved (Figure 5).

Figure 4: Persistence of few lesions after 12 weeks of treatment with subcutaneous IFN alpha 2b.

Figure 5: Complete resolution of the dermatosis after 12 weeks of treatment with subcutaneous IFN alpha 2b + 4 weeks of topical podophyllin 0.5%.

Discussion

Currently, there is no specific antiviral treatment that cures HPV infection. Existing therapeutic modalities focus on the destruction or elimination of visible lesions or the induction of cytotoxicity in infected cells (Table 1).

Cryotherapy is one of the most commonly used treatments. It is based on tissue destruction through necrosis produced with liquid nitrogen at low temperatures (-196°C). The technique consists of applying complete freeze-thaw cycles, which vary depending on the type of lesion, although there is no evidence from clinical trials comparing the number of applications that are most effective. Small blisters usually appear after treatment, which re-epithelialize in 1 - 2 weeks. Scarring, altered sensation, or pigmentary changes rarely occur as sequelae [11, 12].

Table 1: Available treatments for condylomata acuminata.

S. no	Treatments
Patient-applied treatment	
1	Imiquimod: 5% cream
2	Podophyllotoxin: 0.5% solution, gel, or cream
Physician-applied treatment	
1	Cryotherapy
2	Electrosurgery
3	Surgical excision
4	Curettage
5	80 - 90% trichloroacetic acid solution
6	25% podophyllin solution
7	IFN

Trichloroacetic acid is a very inexpensive caustic agent that destroys warts through chemical coagulation of proteins. It is especially useful for small warts and those on mucosal and semi-mucosal areas. It is used at a concentration of 80 - 90%, with clearance rates of 56 - 81% after 2 - 6 sessions and recurrence in 36% of patients. Side effects are very rare. After application, the patient may experience burning pain and impaired wound healing [11, 12]. Genital warts can also be destroyed by electrocautery, although extreme care must be taken due to the volatilization and possibility of aspiration of viral particles [11]. In mild cases, with fewer than 3 lesions, monotherapy, such as cryosurgery or topical trichloroacetic acid, is a reasonable choice, while sequential treatment is more effective in more severe cases [13]. Surgical treatment may be considered for large, pedunculated lesions, as well as for difficult locations such as the urethral meatus, intra-anal area, intravaginal area, or cervix [14]. Due to the large number and size of the lesions, we did not consider any of the destructive treatment options as first-line therapy for our patients.

Non-destructive medical treatments include podophyllotoxin, imiquimod, and IFN.

Podophyllotoxin 0.5% cream or gel is an effective, but irritating, cytotoxic drug. It is applied to palpable external warts twice daily for 3 days, followed by a 4-day rest period, repeating the same regimen for up to 4 cycles [12]. Imiquimod is an immune response modifier that stimulates the production of alpha-IFN, tumor necrosis factor, interleukin (IL)-1, IL-6, IL-8, and other cytokines. For the treatment of genital warts, it is used as a 5% cream, applied 3 times a week (Monday, Wednesday, and Friday) for up to 16 weeks [15]. IFN is a useful and effective treatment for patients with multiple warts, whether genital or in other locations. IFN refers to a group of naturally occurring glycoproteins with antiviral, antiproliferative, and immunomodulatory properties. Three main classes have been identified: alpha, beta, and gamma. IFNs have shown antiviral properties against HPV both in vitro and in vivo. They have been shown to protect murine cells against bovine papillomavirus infection and to eliminate extrachromosomal viral DNA from infected cells [16]. Numerous regimens exist regarding the dosage, route, and duration of IFN administration for the treatment of genital warts.

In cases of multiple and large warts, as in our patient, systemic IFN is a useful, effective, well-tolerated therapeutic option with few adverse effects.

The Food and Drug Administration-recommended regimen is IFN alpha 1 to 3 million IU, 5 times a week for 2 weeks, followed, if necessary, by 3 doses per week for 4 weeks, administered intramuscularly or subcutaneously [9]. In our division, we have experience treating numerous patients with multiple genital warts using a regimen of 1.5 to 3 million IU of IFN-alpha weekly, administered subcutaneously for 12 weeks. This was the regimen chosen for our patient, in whom we observed a very satisfactory response [12]. Persistent infection with high-risk oncogenic types of HPV can progress to cervical, other genital, and oropharyngeal cancers. The vaccine against this virus thus becomes a fundamental tool for primary prevention [17].

Regarding vaccination, a meta-analysis was found that addresses the global impact of HPV vaccination [11]. It shows a significant decrease in the incidence of anogenital warts with the use of vaccines, as well as in low- and high-grade neoplasms in women, in addition to a significant herd immunity effect in the population. Therefore, HPV vaccination is strongly recommended for the prevention of HPV-related infections [11]. According to national guidelines, the AUGE guide for cervical cancer in 2015 recommends vaccinating girls between 9 and 13 years of age with two doses (at 0 and 12 months) [4]. However, the National Immunization Plan, starting in 2019, also includes boys in the vaccination schedule [12].

Conclusions

Multiple genital warts pose a challenge for physicians due to the physical and aesthetic alterations they cause in patients and the therapeutic difficulties involved, in addition to the possibility of malignant transformation depending on the causative HPV genotype. The existence of numerous therapeutic modalities reflects that none is completely effective, so many patients require more than one treatment (combination therapy). Most treatments (cryosurgery, electrocoagulation, laser, acid application) aim at destroying the warts and can be painful, which limits their use in some patients. IFN alpha 2b, applied subcutaneously at doses of 1.5 to 3 million IU per week for 12 weeks (depending on the therapeutic response), represents a highly effective, accessible, minimally invasive, low-adverse-effect, and cost-effective option for patients with multiple warts who have not responded to or cannot tolerate other treatments. HPV vaccination represents a crucial tool in the prevention of various associated neoplasms, and its global implementation remains essential to reduce the burden of these diseases in the population, particularly in young people and at-risk groups.

Acknowledgments

None.

Conflict of Interest

None.

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