

Therapeutic protocol of vulvar and cervical HPV-Infection

**R. Zarccone, M.D., P. Bellini, M.D., E. Carfora, M.D., M. Monarca, M.D.,
G. Vicinanza, M.D., A. Cardone, M.D.**

2nd University, Department of Obstetrics and Gynecology, Naples - Italy

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Summary

Background: The stages of HPV (Human Papilloma Virus) infection are under the control of the immune system, which is inhibited by the virus itself. Thus, at present the treatment of condyloma acuminata is based on the use of interferon (IFN).

The aim of the present study was to evaluate immune system activation and clinical response to IFN therapy. In addition, in the most serious cases, medical treatment with IFN was associated with diathermocoagulation (DTC) of persistent warts. The effectiveness of the combined therapy was also assessed.

Methods: 7 women (age range: 16-52) suffering from cervix condylomata were selected for our study. All of them were injected intramuscularly with doses of 3 milion UI of IFN- α leucocyatar every three days for six weeks together with daily applications of α -IFN for six weeks.

The women that were still ill three months after IFN therapy, were treated with DTC. In one case, another cycle of IFN treatment was necessary.

Results: Clinical response to IFN treatment was complete in 46 cases, partial in 20 cases and unsuccessful in 4 cases. After three months of medical therapy, 30 women were treated with DTC. After this therapy, in 21 cases, the warts were resolved. After 24 months the percentage of relapse was 37.9% when only IFN was used, and 4.51% when IFN was combined with DTC.

Conclusions: These data suggest that a successful protocol for the treatment of condyloma acuminata consist of IFN therapy associated with DTC when warts persisted.

Key words: Condyloma acuminata; Interferon; Diathermocoagulation.

Introduction

Until a few years ago the therapy of condyloma acuminata was based exclusively on physical intervention, such as surgical exsection, lasertherapy, cryotherapy, DTC or topical drug remedies e.g., 5-fluorouracil or trichloroacetic acid. These methods proved quite painful and did not completely prevent relapse [1, 2, 3]. Therefore, further studies have been carried out in order to find out a more effective therapeutical protocol.

These studies rely on the evidence that condylomatous lesions are histologically characterized by a virus-induced modification in the epithelial microenvironment, accompanied by inhibition of the migration of the cells involved in the immune response (CD1+, CD4+, CD8+) [4]. It has been demonstrated that the stages of HPV infection are under the control of the immune response, which is inhibited by the virus itself. Consequently, at present the medical treatment of condylomata acuminata of the cervix employs IFN [5].

The most useful IFN for the treatment of condylomata of the cervix is natural alpha-IFN, subsequently recombinant alpha-IFN has also been used.

IFN can be administrated either by (intramuscular or subcutaneous) injection or by topical application; several therapeutic protocols have been used.

The aim of our investigation was to evaluate both the immune system arousal and clinical response to IFN therapy in women afflicted by vaginal condyloma, as well as to assess the effectiveness of IFN treatment used either alone or combined with physical therapy.

Materials and Methods

This study included 71 women who had been subjected to Pap-Tests and colposcopy at the outpatient department of Gynecological Oncology of the Institute of Gynecology and Ostetrics at the 2nd University of Naples. Forty of them were affected by vulvar microcondyloma, 20 by cervical and vulvar condyloma and 11 by condyloma associated with CIN.

All patients were subjected to the following treatment: 3M IU of Alpha-interferon or 3M IU of Recombinant-interferon A injected intramuscularly twice a week for six weeks in association with the topical application of Alpha-interferon cream daily for six weeks.

The patients with persisting lesions three months after the end of the treatment were subjected to DTC. Finally, the cases with incomplete resolution of the lesions after 3-6 months from DTC, were subjected to a second cycle of IFN therapy.

The clinical response to the therapy was evaluated by colposcopic, colpocytologic and histologic examinations.

Results

After the first cycle of IFN, a total response to the therapy was observed in 46 patients (64.78%), a complete response, with considerable remission of the symptoms and persistence of the keratinized lesions, in 20 patients (28.17%), and a partial response or no response in five patients (7.04%). The 25 patients showing partial or unsuccessful response or persistence of keratinized lesions were subjected to DTC after three months after drug therapy. In 21 cases (84.00%) recovery was complete after DTC. In four cases (16.00%) resolution was

partial, and the patients were subjected to another cycle of IFN with resolution of the warts (Tab. 1).

After 12-24 months, the percentage of relapse was 37.9% for the cases treated only with one cycle of IFN and 4.51% for those treated with one cycle of IFN and DTC. The patient treated with two cycles of IFN and DTC did not relapse (Tab. 2).

Table 1. — *Clinical response to treatment*

Type of response	1 st IFN-cycle		DTC		2 nd IFN-cycle	
	n. of cases	%	n. of cases	%	n. of cases	%
Total	46	64.78	21	84.00	1	100
Partial	20	28.17	4	16.00	0	0
Absent	5	7.04	0	0	0	0

Table 2. — *Follow-up after 24 months*

Type of treatment	% of relapse
1 st IFN-cycle	37.9
1 st IFN + DTC	4.51
1 st IFN-cycle + DTC + 2nd IFN-cycle	0

Discussion

Our results showed a significant clinical response to IFN therapy. Though drug therapy does not always cause complete resolution of Papilloma virus infection it is a relevant adjuvant treatment to physical therapy, remarkably increasing the percentage of therapeutic success [6]. Some investigators have studied the role of Interleukin 2-r in modifying the immune response.

In fact, interleukyn-2r induces cell replication and the functional maturation of lymphocytes T, has a regulatory action on lymphocytes B and induces the proliferation of natural-killer cells [7].

A comparison of the results obtained by combining IL-2 and leucocytic α -IFN with those obtained with only IFN therapy clearly shows that the former causes an

increase in the antiviral, cytotoxic and antineoplastic activity, with a consequent greater response to the therapy [8, 9].

However to conclude, cervical condyloma is one of the most widespread venereal diseases [10]; it is induced by HPV, the oncogenic effects of which have been well-demonstrated *in vitro* [11]. Therefore, great importance is being attached to new therapeutic protocols leading to a higher percentage of recovery.

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Address reprint requests to:
PRIMULA BELLINI, M. D.
Via Cappuccini, 16
82016 Montesarchio (BN)
(Italy)