

Treatment of cervix condylomata with Alpha-IFN leucocytar

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Summary: The main viruses responsible for condyloma, a venereal disease, are the HPV 16 and 11. The stages of HPV infection are under the control of the immunitary system, which is inhibited by the virus itself. For this reason, the therapy of cervical condylomatosis is, at present, based on the use of interferon.

The purpose of this study was to appreciate the activation of the immune system after therapy with interferon. We treated 12 women suffering from cervical condyloma and exocervical CIN with increasing doses of natural alpha-IFN injected intramuscularly, and also applied to the vagina.

The clinical response to the therapy was total in 7 cases, partial in 4 cases and unsuccessful in 1 case. We also evaluated the percentage of inflammatory cells in the peripheral blood and at the level of the condylomatous lesions. After treatment the absolute and percentage number of inflammatory cells increased. Besides, at the level of the lesion the CD1 and CD4 cells also increased.

Key words: Cervix condyloma; Therapy; Alpha-Interferon.

INTRODUCTION

Condylomata are probably of viral origin. HPV 6 and 11 are considered the main viruses responsible for this venereal disease⁽¹⁾. They belong to the family of the Papova virus, and are able to stimulate the activation of invasive neoplasia in vitro. Clinically, condylomatous lesions are frequently associated with cervical intraepithelial neoplasia (CIN) and

that confirm the risk of neoplasia related to HPV infection⁽²⁾.

All the stages of HPV infection are under the control of the immunitary system, which is inhibited by the virus itself. This is corroborated by histological examination of condylomatous lesions. They appear characterized by virus-induced modifications of the epithelial environment, with inhibition of the migration of accessory cells, especially Langerhans cells, which are also reduced in number. In fact, an increase in their number at the level of the lesions is considered as a positive prognostic marker⁽³⁾.

For this reason, at present, the therapy of cervical condylomata is based on the use of interferon (IFN)⁽⁴⁾.

Interferons were first isolated by Isaacs and Lindermann in 1957. They were

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identified as glycoproteins produced by cells in response to invasion by a virus, and were able to interfere with virus replication acting on a gene, carried on chromosome 21, which can synthesize antiviral proteins ⁽⁵⁾.

It is now generally agreed that they can also inhibit cancer development, and have an immunomodulating action ⁽⁶⁾.

Interferon is fundamental to an effective cell-mediated immune response, and hence plays a primary role in the virus-organism relationship ⁽⁷⁾.

The aim of the present study was to assess the activation of the immune system following therapy with IFN.

MATERIALS AND METHODS

Our investigation was conducted on 12 women of 22 to 48 years suffering from cervical condylomata and exocervical CIN. They were subjected to cytological and histological examination, colposcopy and biopsy for papillomavirus detection and typing by an *in situ* hybridization (ISH) assay using the DNA probe. In all of the cases, HPV (8 cases HPV 6 and 4 cases HPV 11) and CIN (in 5 cases CIN II and in 7 CIN I) were found (Table 1).

In addition, 4 patients with low grade lesions were subjected to the same examinations, as a control group.

With the patients' consent, increasing doses (1.000.000-3.000.000 UI) of natural alpha-IFN (Alfa Wasserman-Italy) were injected intramuscularly for 3 weeks. In the last two weeks, alpha-IFN cream was also applied to the vagina by a special cannula.

For the assessment of IFN action, the following parameters were determined:

i) Absolute and per-centage number of lymphocytes and eosinophils (before and after treatment).

ii) The DR receptor by flow cytometry, using monoclonal antibodies labelled with fluoresceine (OKTDR) in lymphocytes from peripheral blood (before and after treatment).

iii) Cell filtrate of the lesion by the immunohistochemical indirect immunoperoxidase method amplified with the strepto-avidin-biotin system, using the monoclonal antibodies OKT4, OKT8, OKT6 reacting with the antigenic determinants CD4, CD8, CD1 (before and after treatment).

Table 1. — *Sample before the treatment.*

	HPV 6	HPV 11	CIN I	CIN II	CIN III
Cases	8	4	7	5	0

The preparations were examined under a fluorescence microscope, and the mean of labelled and unlabelled cells was calculated in five microscopic ranges at high magnification (400x).

RESULTS

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

When the regression of the lesion was complete, the response was considered total (TR), in the presence of at least a 50% regression, partial (PR), and when the lesion remained unchanged the response was considered unsuccessful (UR).

Before the treatment, the absolute and percentage number of lymphocytes and eosinophils was below the standard. After the treatment the absolute and percentage number of lymphocytes and eosinophils increased by 20% and 80%, respectively.

A 20% increase was also observed in the DR-receptor (Table 2). Before the treatment the cells CD1 (Langerhans

Table 2. — *% increase of the parameters indicating responsiveness of the immune system.*

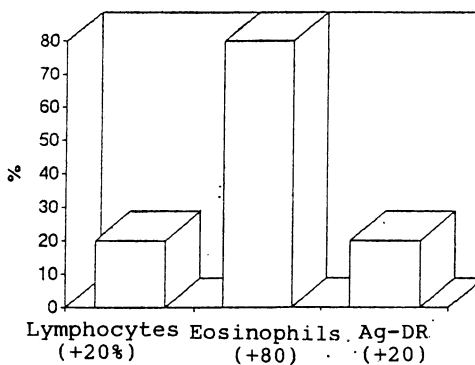
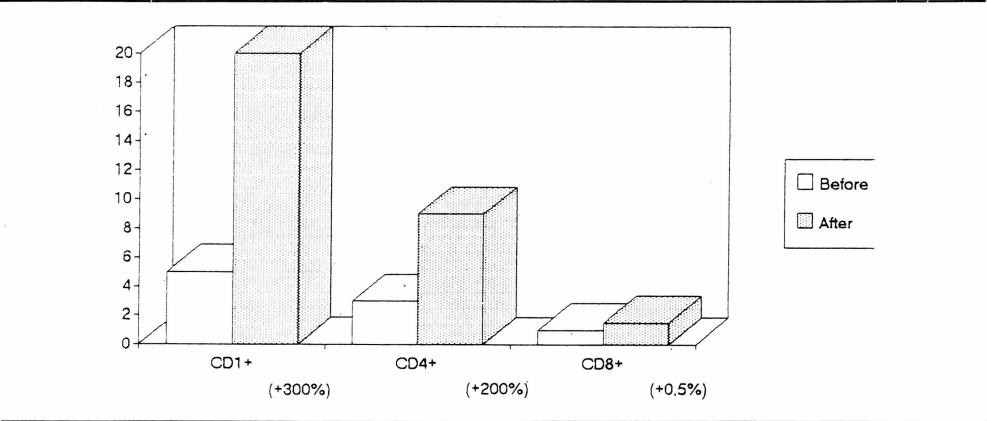


Table 3. — Modifications of cells CD1+, CD4+, CD8+ after therapy with α IFN.



cells), CD4 (T helper lymphocytes) and CD8 (T suppressor lymphocytes), in histological preparations at high magnification (400x), were 5%, 3%, 1%, respectively. After the treatment the increase in

CD1 and CD4 cells was 300% and 200%, respectively.

The percentage of CD8 cells, instead, remained almost unchanged (Table 3).

No variation was observed in the control group.

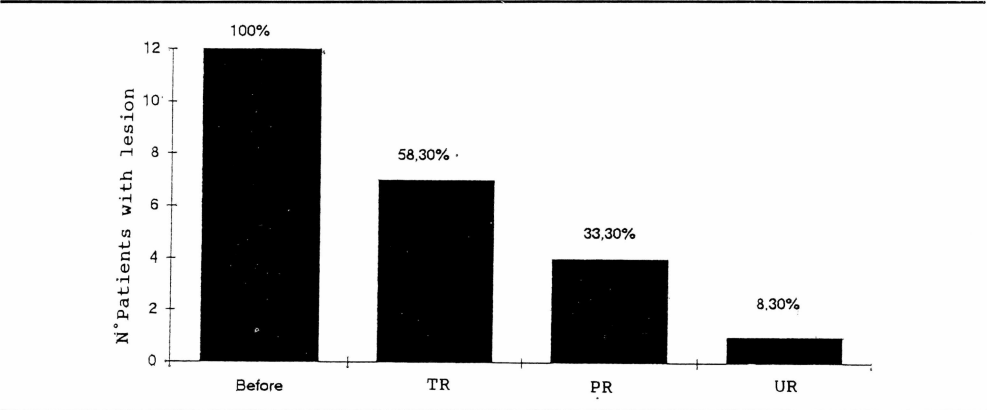
After 7 days from the end of the treatment, the response to the therapy was total in 7 cases (58.3%), partial in 4 cases (33.3%), unsuccessful in 1 case (8.3%) (Tables 4 and 5).

Clinically detectable symptoms disappeared at the beginning of the treatment.

Table 4. — Response to the therapy after 7 days.

Type of response	Cases	%
TR	7	58.3
PR	4	33.3
UR	1	8.3
Total	12	100

Table 5. — Clinical effectiveness of the therapy.



DISCUSSION AND CONCLUSIONS

A reduction in the number of the Langerhans cells (CD1+) was well demonstrated at the level of HPV-induced condylomatous lesions⁽³⁾.

Though based on a small sample, our investigation has shown a significant increase in the number of the CD1+ cells at the level of the lesions. It has also evidenced an increase in the expression of the DR-antigen which is fundamental to the activation of CD4+ cells, and hence to all cell-mediated immune response.

To obtain a deeper insight into the IFN effect, some authors have studied its immunomodulating action. An immunosuppressive action has been suggested at high concentrations, which might prevail over its antiviral action. To avoid this negative effect association of IFN with Interleukin-2r is being tested and the results appear promising^(8, 9).

So far, the treatment of condylomata with IFN appears desirable, since it is not only able to have positive effects on clinically detectable lesions, but also to prevent and cure viral infections, even in the absence of physical therapy.

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