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Immunologic Profile of Patients Suffering from Herpes Simplex Virus (HSV) -Associated Oral Lesions Treated with Natural Human Interferon Alpha (Egiferon)

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10 consecutive patients with HSV-associated chronic oral lesions were treated with Egiferon for ten days. There were a statistically significant increase in the Large Granule Lymphocyte (LGL) counts and the number of spontaneous E rosette forming cells by the end of the treatment period. Interferon alpha

brought about a preferential expression of CD8, CD11b, CD14, CD25 and CD45RO cell surface molecules without any effect on the expression of CD2, CD3, CD4, CD20 and HLA-DR. (Pathology Oncology Research Vol 3, No 1, 44-46, 1997)

Key words: interferon alpha, herpes virus, lymphocyte subpopulations

Introduction

Human interferon alpha extracted from buffy coat was the first interferon available on a large scale for clinical use.⁴ Since 1960 antiviral, antiproliferative and immunoregulatory properties of interferons have been abundantly studied^{2,5,7,10,14,15,20} and exploited for treating a large spectrum of human diseases, chiefly haematological malignancies.^{6,8,16,22,23} Recently, however, successes have also been achieved in some chronic viral diseases with interferon treatment.^{1,3,9,10,21} These favorable results encouraged us to give interferon to patients suffering from recalcitrant oral HSV-associated disorders.¹³ We present here the findings on phenotypic changes of circulating mononuclear cells of our patients treated with Egiferon.

Patients and Methods

Three men and seven women (mean age 36.2 years) with serologically confirmed¹⁹ HSV-associated recurrent oral disorders were tested. The patients gave informed consent

for participation. The study was approved by the Ethical Committee of the Semmelweis University of Medicine.

Natural human interferon alpha (Egiferon) was manufactured by EGIS Pharmaceutical Company (Hungary). The patients were given 1 million I.U. Egiferon daily for ten days.

The number of peripheral blood lymphocytes (PBL) and LGL were counted under the light microscope.

Mononuclear cells were separated on Ficoll-Uromiro gradient. The "total" and "active" E rosette forming PBL were determined by the appropriate assays.^{11,24}

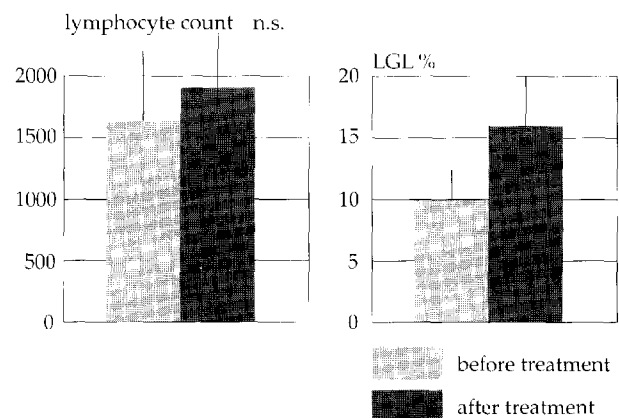


Figure 1. An increase in the LGL count ($p < 0,01$) took place following interferon treatment, whereas the number of PML has not changed

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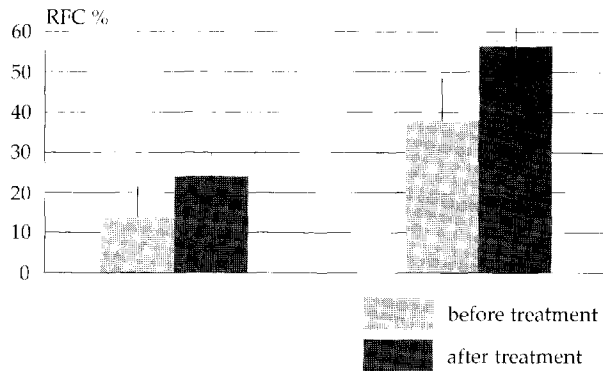


Figure 2. Interferon increased the "active" and the "total" RFC counts ($p < 0,01$)

CD2, CD3, CD4, CD8, CD11b, CD14, CD20, CD25, CD45RO, and HLA-DR cell surface molecules (Ortho and DAKO) were defined by using Ortho Cytrome Absolute Flow Cytometry, and OPD4¹⁷ monoclonal antibodies.

All these assays were performed before and 10 days after the completion of Egiferon treatment.

The double Student's "t" test was used for statistical evaluation of the data.

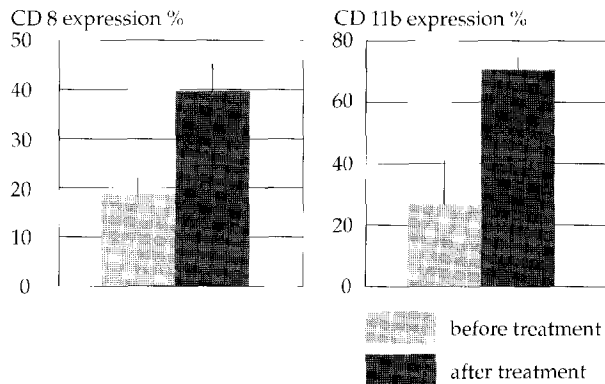


Figure 3. Preferential expressions in CD8 ($p < 0,005$) and CD11b ($p < 0,001$) took place after interferon treatment

Results

The absolute lymphocyte counts showed individual variations, being increased in seven cases and unchanged in three. The overall increase, however, was not statistically significant. On the other hand Egiferon induced statistically significant elevation ($p < 0,01$) in the number of LGL cells (Fig.1). Both the "active" and "total" E rosette forming cells (RFC) showed statistically significant increase ($p < 0,01$) at the end of interferon treatment (Fig.2).

There was no remarkable change in the expression of CD2, CD3, CD4, CD20, and HLA-DR, whereas statistically significant increase was found in the expression of

CD8 ($p < 0,005$), CD11b ($p < 0,001$) (Fig.3), CD14 ($p < 0,001$), CD25 ($p < 0,001$) (Fig.4) and CD45RO ($p < 0,01$) (Fig.5).

Discussion

Ten otherwise healthy patients with recurrent HSV-associated oral mucous lesions were treated with natural human interferon alpha (Egiferon) for ten days. The beneficial clinical effect of this treatment¹³ was accompanied by particular changes in the expression of various

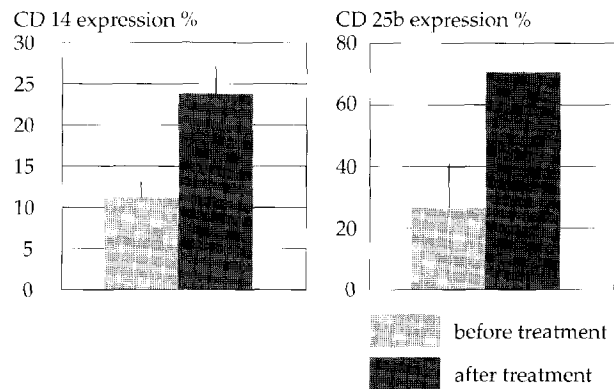


Figure 4. CD14 ($p < 0,005$) and CD25 expressions increased after interferon treatment

mononuclear cell markers. Before Egiferon treatment the marker pattern of the whole Ficoll-Uromiro-isolated PBL population showed no abnormalities based on the detection of pan-T CD2 and CD3 and the subset-specific CD4 and CD8. As a result of 10 day interferon administration, however, there was a considerable increase in the number of LGL cells, surface expression of cytotoxic T cells and a subset of NK cells (CD8), of activated LFA-1 beta chain carrying cells (CD11b), of monocyto-macrophages (CD14), of IL-2 receptor positive activated lymphocytes

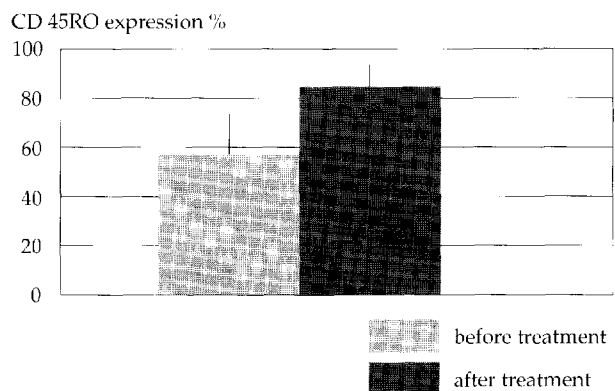


Figure 5. An enhancement was found in the CD 45RO expression as a result of interferon treatment ($p < 0,02$)

(CD25) and of the majority of Th1 lymphocytes (CD45RO). Similar positive changes were detected in the number of "active" E rosette forming PBL that may represent a subset of activated T cells.

The changes in the expression of cell surface markers may be a reflection of the generation of activated peripheral mononuclear cells brought about by the natural interferon alpha. Moreover, stimulation by interferon alpha of these mononuclear cell subsets can be used as laboratory correlates of the *in vivo* therapeutic efficacy of Egiferon. The increased activity of cytotoxic T cells, the lineages of macrophages and LGLs and of activated Th1 cells suggest that at least part of interferon alpha's advantageous clinical effects are brought about via the contribution of these cells. Our results somewhat differ from those of patients with chronic active hepatitis B treated with interferon alpha 2b where NK and activated cells were significantly increased before and were gradually decreased by the end of the treatment.¹⁸ The difference may be attributable to the type of interferon alpha produced by genetic engineering and the dosage.

Taking into account that immunomodulation by interferons *in vivo* is a rather complex process, our attempt to monitor some surface marker changes can be regarded only as a first step in evaluating the cellular immune profile of patients suffering from chronic HSV infection and treated with interferon alpha. Our preliminary data may lead to more thoroughly performed clinical and laboratory studies because interferon treatment of chronic oral virus related diseases is not yet widespread. No larger clinical trial has been published.

It is of primary importance to note that natural interferon alpha showed several advantageous properties as it did not decrease peripheral cell counts in this dosage, and its effect on PBL was unanimously stimulatory without any depressive side effects.

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