Electron-Microscopic Study of Plasma Cells from Regional Lymph Nodes of Rats After Topical Interferon Administration

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Transmission electron microscopy of plasma cells from soft strands of cranial deep cervical lymph nodes removed from male Wistar rats at different times after their intranasal treatment with an aqueous α-interferon solution showed a decreased volume of the Golgi complex and lowered numbers of ribosomes and mitochondria in both mature and immature plasma cells. The results of the study are tentatively interpreted as indicating reduced energy potentials and antigen-synthesizing capabilities of the plasma cells formed *de novo* after α-interferon treatment.

Key Words: *lymph nodes; interferon; plasma cells*

Interferons (IFNs) and, in particular, α-IFN were previously thought to be capable of conferring only resistance to viral infections. However, as the experience gained with their application in various dosage forms has shown, IFNs hold considerable promise for use in a number of acute or chronic infections, neoplastic diseases, and other conditions.

α-IFN raised immunoglobulin levels in the blood serum of animals with viral hepatitis B, but did not alter the immune response of B lymphocytes when added to their culture [3]. α-IFN appears to influence antibody synthesis by modifying the function of helper T cells which were found to have 65 receptors to α_2-IFN alone [4-6]. According to some experimental findings [9], IFNs of all types can stimulate the proliferation of activated B cells. On the other hand, there is evidence that neither proliferative nor functional activity of resting or activated B cells is stimulated by any IFN type [8]. Moreover, α-IFN was reported even to inhibit the proliferative activity of stimulated B cells from patients with leukemia, the inhibition being enhanced by added glucocorticoids [10].

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In general, the impact of α-IFN on cells of the plasmacytic series has been studied inadequately, the relevant experimental data are scarce and contradictory, and next to nothing is known about how different IFN types affect the ultrastructure of these cells. The purpose of the present study was to examine, by means of transmission electron microscopy, the ultrastructural organization of plasma cells in rats after their topical treatment with α-IFN.

MATERIALS AND METHODS

The study was conducted on male Wistar rats (body weight 180-200 g). Test rats received a recombinant human α_2-IFN (reaferon) diluted with distilled water to a concentration of 50 U/ml; two drops of this solution were administered intranasally to each rat four times daily for 5 days. Control rats received distilled water by the same route.

Regional lymph nodes (cranial deep cervical nodes) were taken from the rats on days 3, 7, 14, and 30 after the last administration of the IFN or distilled water (30 animals were used per experimental point).

For transmission electron microscopy, the lymph node material was fixed in a 1% OsO_4 solution in

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phosphate buffer (pH 7.3), dehydrated through graded ethanol concentrations, and embedded in Epon. Semithin sections were then prepared on an ultramicrotome, stained with toluidine blue, and used to select the lymph node area required for examination. The ultrathin sections produced were counterstained with uranyl acetate and lead acetate and examined in a JEM-100S electron microscope. Plasma cells were identified using a previously proposed classification [1]. The negatives obtained were subjected to a stereological analysis, followed by statistical treatment of the results. Differences between the mean results were considered significant at the $p<0.05$ level by Student's t test.

RESULTS

Morphometric parameters of immature and mature plasma cells from soft strands of cranial deep cervical lymph nodes are shown in Tables 1 and 2, respectively.

The contracted volumes of the cytoplasm, mitochondria, rough endoplasmic reticulum, and Golgi complex and the decreased abundance of ribosomes and mitochondria observed in immature plasma cells on day 3 after the last IFN administration, when the number of plasma cells themselves was greatly increased [2], appear to indicate that the newly formed cells had a reduced protein-synthesizing (antigen-synthesizing) capacity. This IFN effect may be presumably attributed to the rapid differentiation of young cells which precluded their adequate maturation.

In mature plasma cells, the rough endoplasmic reticulum was of increased volume on days 3 and 7 after the last IFN administration, whereas the volume of the Golgi complex was decreased, as was the number of ribosomes and mitochondria on days 3, 7, and 14 (cf. Figs. 1 and 2). Possibly, much more antibodies were synthesized by plasma cells and evacuated at accelerated rates from their membranes under the action of reaferon.

The decreased mitochondrial abundance in plasma cells appears to be an indication of their diminished energy potential. It may be that mitochondrial numbers also decrease in cells of other types after their exposure to α-IFN.

TABLE 1. Morphometric Parameters of Immature Plasma Cells from Soft Strands of Cranial Deep Cervical Lymph Nodes in Rats at Different Times after a Cycle of Intranasal Interferon (IFN) Treatment ($M\pm m$)

Parameter measured	Control group	Days after the last IFN injection			
		3	7	14	30
Cytoplasm, *A*	56.4±4.5	41.1±3.6*	39.9±3.6*	40.1±3.6*	35.3±3*
Nucleus, *A*	52.2±4.4	49.9±4.4	49.5±4.6	50.2±4.2	52.8±4.8
Ribosomes, *N*	2339±202	1326±123*	1349±131*	1010±102*	1905±168
Rough endoplasmic reticulum, *A*	5.8±0.25	3.5±0.34*	3.4±0.35*	2.4±0.22*	5.5±0.38
Golgi complex, *A*	4.1±0.74	2±0.11*	1.9±0.3*	2.1±0.19*	4.8±0.25
Mitochondria, *A*	7.1±0.64	4.6±0.48*	4.1±0.34*	1.8±0.18*	6.9±0.31
N	9.6±0.88	4.7±0.47*	4.8±0.44*	3.4±0.38*	6.4±0.33*

Note. Here and in Table 2: *A* = area of the section profile of the structure studied, μ^2; *N* = number of structures within the *A* of the cytoplasm. *$p<0.05$ in comparison with the control group.

TABLE 2. Morphometric Parameters of Mature Plasma Cells from Soft Strands of Cranial Deep Cervical Lymph Nodes in Rats at Different Times after Intranasal Interferon (IFN) Treatment ($M\pm m$)

Parameter measured	Control group	Days after the last IFN injection			
		3	7	14	30
Cytoplasm, *A*	55±4.8	54.7±4.8	53.2±5.8	50.8±5.2	74.5±6.7*
Nucleus, *A*	46.8±4.4	46.7±4.4	46.8±3.7	46.9±4	47.3±4.8
Ribosomes, *N*	1883±172	1148±114*	1372±124*	859±84*	1481±147
Rough endoplasmic reticulum, *A*	21.6±1.9	30.1±3.1*	29.3±3.1*	22.2±1.8	33.5±3.4*
Golgi complex, *A*	10.9±0.88	6.8±0.34*	8.1±0.98*	5.6±0.26*	14.7±1.1*
Mitochondria, *A*	7.6±0.58	9.1±0.98	9.1±1	11.3±0.63*	8.8±0.6
N	8.2±0.46	4.7±0.28*	5.6±0.88*	4.4±0.39*	10.4±0.64*

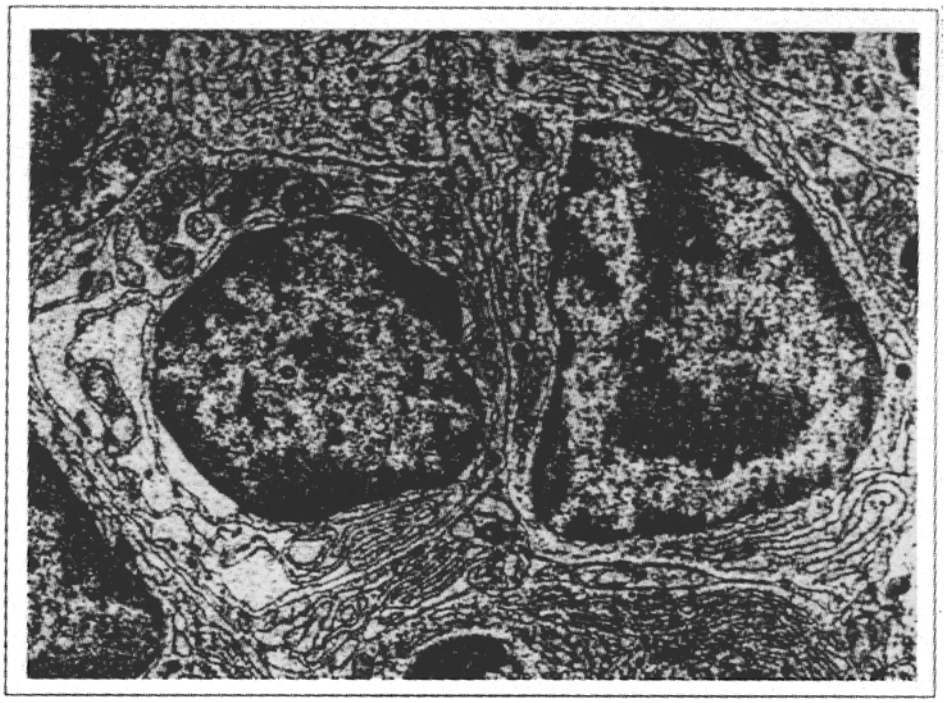

Fig. 1. Mature plasma cells from a soft strand of a cranial deep cervical lymph node before interferon administration. ×7500.

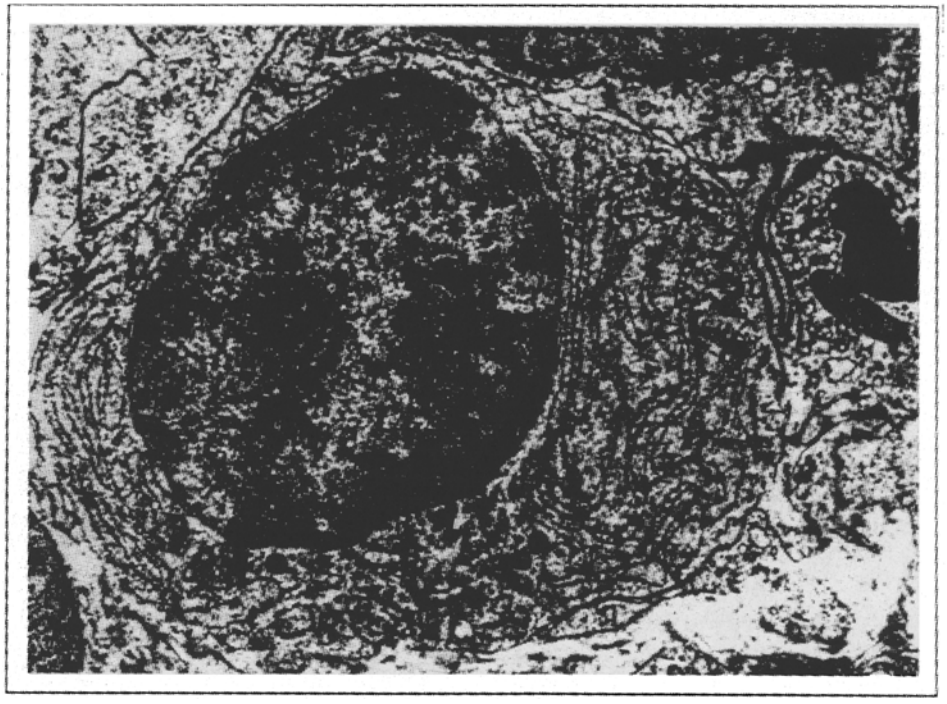

Fig. 2. Mature plasma cell from a soft strand of a cranial deep cervical lymph node 14 days after the last interferon administration, showing decreased numbers of ribosomes and mitochondria in the cytoplasm. ×9500.

The elevated values of most of the morphometric parameters in mature plasma cells on day 30 after the last IFN administration in comparison with their control values, were most likely due to the cessation of IFN action by that time. If so, then immunoglobulin synthesis may be expected to reach its peak only a long time (a month or more) after the administration of an α-IFN preparation such as reaferon [3]. This suggests that the use of α-IFN preparations to enhance the immune response may be inappropriate as an emergency preventive measure during outbreaks of infectious diseases or for the treatment of rapidly progressing diseases. Such preparations may be recommended for use as adjuvants in routine vaccinations.

A possibility, however, exists that the changes we recorded were all due to the α-IFN acting as an antigen of protein nature rather than as an immunomodulator. Indeed, evidence for the ability of all (or at least some) young plasma cells to produce anti-IFN antibodies has been provided [7].

It may be concluded that the rapid reaction of plasma cells in response to IFN probably increases their antigen-synthesizing capacity.

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