EFFECT OF INTERFERON ON METASTASIZATION OF BROWN-PEARCE CARCINOMA

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When injected into rabbits with transplanted Brown-Pearce carcinoma after removal of the primary tumor, interferon inhibits the development of metastases.

Reports of the inhibitory action of interferon on propagation of oncogenic viruses and on the cellular transformation induced by these viruses have recently appeared in the literature [5-7, 9, 10]. In a paper by Wheeloch and Dingle [10] the first mention is made of the good results obtained by induction of endogenous interferon in the treatment of acute myeloid leukemia in man.

The object of the present investigation was to study the effect of interferon on metastasization of tumors.

EXPERIMENTAL METHOD

The Brown-Pearce rabbit carcinoma was chosen as the experimental tumor model, because it is extremely suitable for the study of metastasization. Experiments were carried out on 29 male rabbits weighing 2.0-2.5 kg. All the animals received an injection of 1 ml of 20% tumor tissue suspension into the right testis. To exclude the effect of the primary tumor on metastasization, the testis together with the inoculated tumor tissue was removed by operation 24 h after transplantation of the tumor. Results obtained previously [1, 3, 4] show that the operation of removal of the primary tumor in the early stages with this particular strain not only does not inhibit but, on the contrary, it activates metastasization.

Concentrated (1:1000) human leukocytic interferon, prepared at the N. D. Gamaleya Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR, was used. A single dose of interferon was injected intravenously daily for 10 days after transplantation into 15 rabbits, 4 rabbits received no injections of interferon, and 10 animals received intravenous injections of physiological saline. The character of metastasization was assessed from the postmortem findings, when the degree of dissemination of metastases in the organs was recorded on a four-point system; all the readings were subsequently added together and the mean intensity of metastasization for the various organs was calculated. The numerical results were subjected to statistical analysis [2].

EXPERIMENTAL RESULTS

Metastases were observed in 6 of the 14 rabbits receiving interferon (one animal was rejected because of its early death), i.e., the index of metastasization was 42.9%. Meanwhile, after removal of the testis with the inoculated tumor material, metastasization was found in 12 of the 14 rabbits, giving an index of metastasization of 85.7%. The intensity of metastasization in the organs of the control group was higher in all the animals than in the experimental group (control 28.6 ± 4.67; experimental 2.6 ± 1.1, $P < 0.001$). The number of organs affected by metastases in the experimental animals was 2.0 ± 0.69, and in the control

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11.6 ± 1.75 ($P < 0.001$). In animals with metastases the index of intensity of metastasization in the control group was 33.3 ± 3.30, and in the experimental group 6.0 ± 1.87 ($P < 0.001$), while the number of organs with metastases in the experimental group was 4.0 ± 1.31, and in the control group 13.5 ± 1.13 ($P < 0.001$). The frequency and intensity of involvement of individual organs by metastases was significantly higher in the control group than in the experimental group. For instance, in none of the six experimental rabbits developing metastases were any found in the liver, and only one rabbit had solitary metastases in the lungs. Meanwhile, in 8 of the 12 control rabbits with metastases massive deposits were found in the liver, kidneys, and lungs, sometimes covering the entire surface of the organ. In the control rabbits receiving physiological saline, only negligible activation on metastasization was observed by comparison with the intact animals.

The results described above are evidence of a marked inhibitory action of interferons on metastasization of a transplantable tumor, with suppression of the hematogenous routes of spread. It is difficult at present to conjecture the mechanism of action of heterogenous interferon on metastasization of the tumor. It is perhaps adsorbed onto the body cells, where it creates conditions unfavorable for the development and propagation of tumor emboli. The possibility cannot be ruled out that interferon stimulates the nonspecific immunological reactivity of the animal, which plays an important role in its antineoplastic reactions; this component of defense, like the others, is known to be depressed during the growth of malignant tumors, as the inhibition of interferon formation by human leukocytes in patients with malignant tumors, lymphatic leukemia, and polycythemia [9] may perhaps indicate.

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