EFFECT OF AUTOANTIBODIES ON FUNCTION OF ORGANS AND GROWTH OF MALIGNANT TUMORS

A. I. Nikolaev, Ch. I. Burshtein, N. K. Muratkhodzhaev, and G. F. Makarov

UDC 616-006.04-092:616-097.5

Autoantibodies in the liver of rats depress their liver function and stimulate growth of sarcoma 45.

* * *

Our previous investigation [4] showed that the sera of animals irradiated with x-rays, and also of animals receiving antibiotics, sarcolysin, and 2-acetylamino-fluorene, contain autoantibodies against the liver. These sera and the autoantibodies isolated from them depress dehydrogenase activity and oxygen absorption by the liver tissues of animals, i.e., they have a cytotoxic effect. Exhausted sera do not possess these properties.

The effect of antiliver autoantibodies on liver function and growth of sarcoma 45 in rats was demonstrated by the investigation described below.

Some workers [1-3, etc.] ascribe a leading role to autoimmune processes in the pathogenesis of cancer. At the same time, it has been shown that antiorgan cytotoxic sera, by depressing the reactivity of the animal body and its compensatory powers, stimulate growth of malignant tumors and influenze the localization of metastases in tissues and organs [3, 6].

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats weighing 90-110 g.

Sera containing autoantibodies against the liver were obtained from irradiated rats (RUM-11 apparatus, dose 600 R) and from animals receiving sarcolysin (five injections, each of 5 mg/kg, at intervals of 72 h) and also the alkaloid heliotrin (5-6 injections, each of 100 mg/kg, at intervals of one week). The rats were sacrificed on the 6th day after exposure to the factors mentioned. Sera of the animals of each series were pooled. Autoantibodies against the liver were detected in them, then isolated and used in the experiments (investigations of the effect of autoantibodies on liver function were carried out with whole sera). Sera from heatlhy rats were used as controls.

The effect of autoantibodies on liver function of the rats was studied by a radiometric method using Bengal rose-I^{131} and a scintillation radiometer with automatic recording of curves (hepatograms) of accumulation of radioactive indicator in the organ (the intensity of accumulation of dye in the liver reflects the function of the polygonal cells of that organ [5]). The rats were fixed and placed under the pick-up of the radiometer so that the liver region was exactly beneath the collimator (cylindrical, diameter of hole 1 cm). The background was first recorded, and while recording continued the radioactive indicator was injected in a dose of 3 μCi into the rat's tail vein. Radiometry of the liver continued for 15 min. The hepatogram thus obtained was the control for that particular rat. After complete disappearance of indicator from the liver (after 3-4 days), 0.3 ml of test serum was injected into the tail vein of these same rats, and the hepatogram was again taken as described above 5 days later.

We also investigated the antitoxic function of the rats' liver by means of Nembutal [7]. The drug was injected intraperitoneally in a dose of 30 mg/kg. This dose did not induce sleep in control rats.

To study the effect of autoantibodies on growth of sarcoma 45, the test sera and autoantibodies isolated from them were injected into the tail vein of rats in a volume of 0.3 ml, and the animals were inocu-

Uzbek Research Institute of Roentgenology, Radiology, and Oncology (Presented by Active Member of the Academy of Medical Sciences of the USSR N. N. Zhukov-Verezhnikov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 65, No. 1, pp. 94-96, January, 1968. Original article submitted March 19, 1966.

TABLE 1. Effect of Autoantibodies on Intensity of Absorption of Bengal rose-I^{131} by Rat Liver and Growth of Sarcoma 45 (M ± m)

Animals from which serum obtained	Intensity of absorption of Bengal rose-I^{131} by rat liver (in mm of height of curve)		1-P*	Weight (in g) of sarcoma 45 in rats injected with					
	before injection of serum	5 days after injection of serum		whole serum	1-P†	extracted autoantibodies	1-P	exhausted serum	1-P
Irradiated rats (titer 1:40)	—	—	—	14.7 ± 1.2	1	13.4 ± 1.4	1	9.3 ± 0.8	0.978
Rats receiving heliotrin (titer 1:40)	44 ± 7.2	15 ± 4.1	1	11.6 ± 1.3	0.999	12.0 ± 1.9	0.992	5.1 ± 0.7	< 0.950
Rats receiving sarcolysin (titer (1:20)	32 ± 2.9	21 ± 2.6	0.987	19.2 ± 2.3	1	10.0 ± 1.3	0.967	4.7 ± 1.2	< 0.950
Healthy rats (control 1)	20 ± 3.4	32 ± 4.9	< 0.950	3.9 ± 1.0	< 0.950	—	—	—	—

*Calculated relative to initial data.

†Calculated relative to weight of tumor of rats receiving physiological saline (5.8 ± 0.6).

lated with sarcoma 45 six days later. On the 18th day of tumor growth the animals were sacrificed and the tumors enucleated and weighed.

EXPERIMENTAL RESULTS

The experimental results are given in Table 1. They show that rat sera containing autoantibodies considerably inhibit the ability of the polygonal cells of the liver of healthy rats to accumulate radioactive dye (by 34-66%); serum of healthy rats has no effect on this process.

In the experiments with Nembutal, the antitoxic function of the liver was disturbed for 20-25 days after injection of the autoantibodies.

The depression of liver function, taking place under the influence of autoantibodies in an organ with considerable powers of compensation, is evidence of the well-marked cytotoxic action of antiliver autoantibodies on this organ.

Sera of the experimental animals and autoantibodies isolated from them stimulated tumor growth by 2-3 times compared with the controls. Exhausted sera, like the sera of healthy rats, did not possess this stimulant action. The slight stimulant action of serum from irradiated rats may evidently be explained by incomplete extraction of the autoantibodies.

Stimulation of tumor growth under the influence of autoantibodies must be considered to be the result of their aggressive action on the organism, lowering its protective properties. Autoantibodies arising during the chemotherapy and radiotherapy of cancer are particularly important, for conditions are then created for the more rapid growth of metastases left behind after the course of the treatment.

Autoantibodies thus possess a cytotoxic effect which is manifested both in tissue culture and in the intact organism. This effect must be taken into consideration during investigation of the pathogenesis of diseases and the development of combined methods of treatment.

LITERATURE CITED

1. H. N. Green, In the book: Mechanisms of Carcinogenesis [Russian translation], Moscow (1961), p. 173.
2. A. Kayano, Proceedings of the 8th International Cancer Congress, Vol. 3 [in Russian], Moscow (1962), p. 329.
3. I. N. Maiskii, et al., Uspekhi sovr. Biol., 55, No. 2, 219 (1963).
4. A. I. Nikolaev, M. Sh. Mil'man, G. F. Makarov, et al., Byull. Éksp. Biol., No. 7, 93 (1967).

5. M. N. Fateeva, Outlines of Radioisotope Diagnosis [in Russian], Moscow (1960).
6. L. L. Khundanova, In the book: Proceedings of a Conference on the Problem: "Allergy and Autoallergy" [in Russian], Baku (1963), p. 260.
7. G. L. Plaa, E. A. Evans, and C. H. Hine, J. Pharmacol. Exp. Ther., 123, 224 (1958).