THE EFFECT OF ANTIGROWTH HORMONE ANTISERUM ON KROCKER'S SARCOMA TUMOR

(UDC 616.988.6-085.363.814.32)

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 60, No. 9, pp. 99-101, September, 1965
Original article submitted May 10, 1964

The fact that the somatotropic hormone stimulates protein synthesis not only in normal tissue but also in malignant growths, has been attracting considerable attention. This was first established in the early 1950's during a study of the development of neoplasms in rats [7] and later during a study of the growth of tumors in mice [9]. It was pointed out that neoplasms did not develop in hypophysectomized animals [6].

It was recently shown that the somatotropic hormone increases the primary growth of sarcoma and the number of metastases [5]. Of special interest is a communication in which it was reported that the introduction of the growth hormone into hypophysectomized patients during the regressive phase of tumor development almost immediately produces in them a new eruption of the cancerous process [8].

It is quite probable that an oversecretion of the growth hormone, in excess of the physiological requirements, and preventing the normal synthesis of tissue protein, can be removed or neutralized not only by hypophysectomy or by radiation therapy, but also by injections of antihormone serum. It was recently reported that antisomatic hormone antiserum retarded somewhat the development of tumors in mice [4]. However, these data were based on only one type of experiment in which the antiblastic effect was determined by the slight but statistically significant difference in the weights of 7-day old tumors.

In the present work we have investigated under different experimental conditions the effect of antisomatotropic antiserum on the development of Krocker's mouse sarcoma throughout the entire life of the experimental animals.

EXPERIMENTAL

Experiments were conducted on mice with Krocker's sarcoma (S-180). A total of 77 mice were used. The antiserum to the human growth hormone was prepared in rabbits by means of microdose immunization [2]. Immediately before the experiments fresh tumor tissue was trypsinized under aseptic conditions by means of a method commonly used in tissue and cell culture [1, 3]. Tumor cell suspensions diluted with normal saline to concentrations of 2.8-3.0 million cells per milliliter were injected in 0.3 ml amounts subcutaneously into white mice weighing 16-18 grams. The animals were divided into groups, each containing approximately 10 mice.

The antiserum was injected intraperitoneally in doses of 0.3 ml 40-60 min after tumor transplantation and subsequently daily for 6-9 days. In another experimental variant, mice received the antiserum in doses of 0.4-0.5 ml two hours after transplantation and daily for 13 days.

Two groups of mice served as controls. One group received subcutaneously normal rabbit serum in doses of 0.4-0.5 ml and the other group (with the tumor transplants) did not receive either normal or antihormone serum.

The criteria for the antiblastic effect were: the period of time after transplantation before the tumor was detected, necrotic and ulcerative changes in the tumors, the weight of tumors in the experimental and control animals on the twenty-fourth day after transplantation and the life span of the animals.

The Effect of the Antisomatotropic Antiserum on the Development of Krocker's Mouse Sarcoma

Experiment No.	No. of mice	Antiserum injection: route	Antiserum injection: dose (in ml)	Antiserum injection: period (in days)	Period after which tumors were noticed (in days)	Weight of tumors on the 24th day (in g)	No. of mice with necrosis of tumors	No. of mice living for: 11–23 days	No. of mice living for: 24–28 days	No. of mice living for: 29–58 days	Mice surviving after 28 days (in %)
1	10	Intraperitoneal	0,3	6	6—7-	—	5	3	2	5	50
2	12	Same	0,3	7	7-	4,30	4	8	2	2	17
3	10	» »	0,3	9	7-	3,65	6	5	—	5	50
4	10	—	—	—	4—5-	9,40	—	8	2	—	—
5	10	Subcutaneous	0,4—0,5	13	7-	2,52	6	6	1	3	30
6	15	—	—	—	4—5-	10,55	—	14	1	—	—
7	10	Subcutaneous	0,4—0,5	13	5-	10,13	—	10	—	—	—

*Normal serum.

Development of necrosis in mice with Krocker's sarcoma after 14-15 days following injection of antisomatotropic hormone antiserum.

RESULTS

As seen from the table in both the experimental series, after intraperitoneal and subcutaneous injection of the antiserum, the tumors in mice appeared on the sixth or the seventh day after transplantation, while in the control animals for both experimental groups the tumors appeared 2-3 days earlier. Thus, from the very beginning there took place a certain degree of retardation in the development of the tumors under the effect of antisomatotropic hormone antiserum. The table shows that in a considerable number of experimental mice there were necrotic areas in the tumor tissue, while in the control animals there were no cases with necrosis. The general appearance of necroses is shown in the literature (figure). Necroses usually appeared on the fourteenth to fifteenth day of tumor development, and towards the twenty-first or the twenty-second day became changed into raw ulcers, which in this case could be regarded as a positive factor signifying the beginning of transformation of the tumor.

On the twelfth to fourteenth day following transplantation there was a significant difference in the size of tumors in control and experimental animals. In mice which had received the antihormone antiserum the tumors were clearly retarded. This difference reached its peak at the time of mass mortality of the control animals. As

seen from the table on the twnety-fourth day the weight of the tumors in the control group was equal to 9.4, 10.13, and 10.55 g, while in the experimental animals which had been injected with the antiserum it was two to four times lower. The tumors were smaller, the longer the antiserum treatment; after a 7-day course the weight was 4.3 g while after a 13-day course it was 2.52 g.

Some American authors observed a considerably smaller difference in the weights of tumors in the control and experimental animals [4]. This may be explained by the fact that these workers terminated their experiments too soon, killing the animals on the seventh day following transplantation, i.e., during the earliest period of tumor growth. During this period of time, as in our experiments, the mice received daily doses of 0.3 ml of the antiserum. Unlike the American workers who had the weight of the tumor as their single criterion of the antiblastic effect of antisomatotropic antiserum, we have evaluated the effect of the antiserum according to several criteria and during the entire life of the experimental animals. Our experimental procedures were also somewhat different. We used trypsinization and counted the cells in the suspensions, while the Americans used fragments of tumor tissue for transplantation.

The last fact showing the antiblastic effect of the antiserum was a significantly longer life span of the experimental animals. As seen in the table on the twenty-third day 80-90% of the control animals died and between the twenty-fourth and the twenty-eighth day the rest died. At the same time, in the experimental group in which the mice received the antiserum, only half of them died on the twenty-third day; after the twenty-eighth day there remained alive 30-50% of these animals, and they died only on the fifty-eighth day following tumor transplantation. We would like to stress that aside from the antiserum in the experimental group and normal serum in the control group the animals were not given any other medication.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
