

ONCOLOGY

THE EFFECT OF VARIOUS DOSES OF IONIZING RADIATION ON THE ANTIGENIC AND BIOLOGICAL PROPERTIES OF BROWN-PEARCE CARCINOMA

COMMUNICATION II. CHANGES IN THE BIOLOGICAL PROPERTIES OF THE TUMOR

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The subject of biological variation in malignant tumors by the influence of ionizing radiation has received insufficient study. In work by Goldfeder [3] it was shown to be possible to change the biological properties of mouse sarcoma 180 by irradiating it in vitro with a dose of 800-2000 r. The results of our previous research [1] demonstrate changes in the biological properties of the ascitic cells of Ehrlich's carcinoma by the action of x-rays on them in vitro.

The aim of the present work was to examine the effect of ionizing radiation, and in particular of x-rays, on the biological properties of the cells of the Brown-Pearce tumor of rabbits.

EXPERIMENTAL METHOD

A suspension of tumor cells from a Brown-Pearce carcinoma was irradiated in vitro with x-rays in doses of 2000, 10,000 and 20,000 r. The method of preparation and the conditions of the tumor suspension were described in detail in our first communication [2].

The experiments were performed on 4 groups of sexually mature male chinchilla rabbits of the same weight and age, with 5 animals in each group.

All the animals were inoculated at the same time intratesticularly with 0.5 ml of a suspension of Brown-Pearce carcinoma cells. The first group of rabbits was injected with a cell suspension irradiated with 2000r, the second — 10,000 r, the third — 20,000 r, and the fourth or control group were given the same volume of a 20% suspension of untreated tumor cells.

EXPERIMENTAL RESULTS

Observations on the inoculated animals showed differences in the clinical appearance of the tumor in the experimental and control groups of rabbits. In the table are given the combined results for each group, showing the duration of survival of the inoculated animals, the times of appearance of the tumor in them, and the numbers of rabbits which died or survived.

It will be seen from the results in the table that the shortest latent period — 4.2 days — was observed in the

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Group of animals	Animal No.	Latent period (in days)	Mean latent period (in days)	Number of rabbits dying	Number of rabbits surviving	Duration of life of rabbits which died (in days)	Mean duration of life of rabbits (in days)
1st-irradiated with 2000 r	1667	6	7.0	2	3	75 38	56,5
	2153	8					
	3222	7					
	3259	5					
	3967	9					
2nd-irradiated with 10.000 r	1485	4	5,6	4	1	45 52 69 40	51,5
	2384	5					
	3186	7					
	3426	7					
	3981	5					
3rd-irradiated with 20.000 r	3595	5	6,4	5	0	18 ¹ 29 47 55 62	48,2
	3610	6					
	3792	7					
	3926	8					
	2362	6					
4th-controls	2382	3	4,2	5	0	30 28 27 24 41	30,0
	2383	5					
	2405	4					
	3446	4					
	3907	5					

* Rabbit No. 3595 died from accidental causes on the 18th day and was not taken into consideration when the mean duration of life of the group was calculated.

Note: In rabbits Nos. 1667, 2153, 3222 and 1485 the tumors were absorbed and the animals are still alive (13 months later).

control group of rabbits. In the animals inoculated with irradiated carcinoma tissue, the latent period was lengthened to 5-7 days. All the animals of the control group died from the tumors, which developed extensive metastases. Their mean duration of survival was 30 days.

In the animals inoculated with irradiated Brown-Pearce carcinoma cells, the tumor was observed to follow a different course, which was evidently related to the inequality of the doses of irradiation.

For instance, the rabbits of the 3rd experimental group, inoculated with cells irradiated with 20,000 r, died from metastases, but their mean duration of life was almost twice that of the control animals, being 51.2 days. In the 2nd experimental group of rabbits, inoculated with tumor tissue irradiated with 10,000 r, four of the rabbits died with obvious tumor metastases, and in one the tumor was absorbed on the 22nd day after inoculation. The mean duration of life of the rabbits in this group which died was 51.5 days. Of the rabbits inoculated with cells irradiated with 2000 r, two died, and in three animals the tumors were completely absorbed after a period of growth.

Statistical analysis showed that the differences in the mean indices of the latent periods of the 1st and 4th, and also of the 3rd and 4th groups were significant ($P=0.008$). The differences between the 2nd and 4th groups were not significant ($P=0.08$). The differences between the mean durations of life of the 2nd and 4th groups of animals were statistically significant ($P=0.01$). Analysis of the results for the 3rd and 4th groups showed that the differences between them were close to significant ($P=0.03$). The significance of the differences between the 1st and 4th groups is undoubted.

The atypical development of the tumor in rabbits inoculated with irradiated material is very characteristic. It was shown by the fact that when the tumor reached a certain stage of development, for example the size of a pea, it decreased in size, showed obvious regression, then increased in size once more and led to the death of the animal.

The appearance of atypical development of the tumor in the experimental groups of animals varied in accordance with the dose of x-rays used to irradiate the original material.

For instance, tumor cells irradiated in vitro with large doses of x-rays (in our experiments 20,000 r), when inoculated intratesticularly, although they caused prolongation of the latent period and of the duration of life of the rabbits, and also temporary partial regression of the palpable tumor, nevertheless led eventually to the death of the animals. The atypical course of development of the tumor in the group of animals inoculated with cells irradiated with 10,000 r hardly differed from that described above.

Tumor cells irradiated with comparatively small doses of x-rays (in our experiments 2000 r), when inoculated intratesticularly, showed a more marked atypical course of the tumor, accompanied in the majority of cases by repeated and considerable regressions of the tumor, even by complete absorption and clinical recovery of the experimental animals. In cases of complete absorption of the tumor (rabbits Nos. 1667, 2153, 3222), a lasting immunity to further inoculation of tumor tissue was observed.

The results obtained demonstrate that the action of x-rays on Brown-Pearce carcinoma cells in vitro causes a change in the biological properties of the tumor cells, and moreover that the intensity of the change shows a definite relationship to the dose of irradiation. In contrast to doses of 20,000 r, in our experiments doses of 2000 r gave the most intensive changes in the biological properties of the tumor cells.

SUMMARY

If intratesticular tissue of Brown-Pearce carcinoma is inoculated in rabbits following irradiation by x-rays in vitro (2000--20 000 r) the biological properties of the tumor cells are altered, the latent period of the tumor development prolonged, the life span increased, and atypical development, and in some cases, even complete resolution of the tumor are observed.

The intensity of the mentioned changes depends directly upon the dose of irradiation.

As compared with a dose of 20,000 r the changes in the biological properties of the tumor cells after irradiation with 2000 r were found to be more pronounced.

LITERATURE CITED

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* Original Russian pagination. See C.B. Translation.