THE EFFECT OF VARIOUS DOSES OF PENETRATING RADIATION ON THE ANTIGENIC AND BIOLOGICAL PROPERTIES OF BROWN-PEARCE CARCINOMA IN EXPERIMENTS IN VITRO

COMMUNICATION I. CHANGES IN THE ANTIGENIC PROPERTIES

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There has recently appeared a comparatively large number of papers devoted to changes in the biochemical properties of cells and tissues under the influence of penetrating radiation [1, 2, 5, 6, 7, 15, 16, 17].

In a number of papers [4, 10, 11, 12, 13, 14] changes have been shown in the antigenic structure of normal tissues under the influence of x-rays.

Arising from the hypothesis put forward by N. N. Zhukov-Verezhnikov, I. N. Maiskii and G. S. Gostev [3] on the character of the antigenic variation of tumor cells under the influence of ionizing radiation, we carried out a series of investigations of the action of x-rays on the antigenic properties of tumor tissues.

In our previous communications [8, 9] we have pointed out changes in the antigenic and biological properties of the cells of a mouse cancer (the ascitic form of Ehrlich's carcinoma) under the influence of x-rays in vitro.

The aim of the present research was to study the variation of the antigenic composition of the cells of the Brown-Pearce rabbit carcinoma under the influence of penetrating radiation (in particular of x-rays) and the relationship between these changes and the dose of irradiation.

EXPERIMENTAL METHOD AND RESULTS

The investigation was carried out on a 20% suspension of Brown-Pearce carcinoma cells, irradiated by x-rays in vitro doses of 2000, 5000, 10,000 and 20,000 r.

The suspension of cells was prepared as follows: in a rabbit affected by a Brown-Pearce tumor, tissue was taken from tumor nodules showing no signs of necrosis, weighed, placed in a sterile Petri dish and cut into small pieces with scissors to obtain a homogeneous mass, physiological saline being gradually added to the dish in proportion of 1:5. The 20% suspension of Brown-Pearce cells thus obtained was poured in volumes of 2.8 ml into glass bottles with a basal diameter of 3.5 cm, and irradiated with x-rays in the doses given above.

Irradiation was given by means of an RUT-60-20 (RUM-7) apparatus. The conditions of irradiation in all the experiments were the following: for a dose of 20,000 r, voltage 60 kv, current 20 ma, filter 0.1 Al, focal distance 75 mm, time of irradiation 36 seconds. For the remaining doses the conditions of irradiation were altered only in respect to the current strength and the time of exposure. For a dose of 10,000 r, for instance, the current was 10 ma and the exposure 37 seconds, and for a dose of 5000 r the current was 5 ma and the exposure 15 seconds.

TABLE 1

Results of the Anaphylaxis with Desensitization Reaction

Sensitization. Antigen — Brown-Pearce carcinoma cells irradiated with 5000 r	Desensitization. Antigen — untreated Brown-Pearce carcinoma cells						Assaulting injection. Antigen — Brown-Pearce carcinoma cells irradiated with 5000 r	
	1st injection		2nd injection		3rd injection			
dose	dose	reaction	dose	reaction	dose	reaction	dose	reaction
0.5	0.2	++	0.35	+++	0.5	—	0.5	++
0.5	0.2	+	0.35	—	0.5	—	0.5	+
0.5	0.2	++	0.35	±	0.5	—	0.5	++
0.5	0.2	+++	0.35	+	0,5	—	0.5	+++
0,5	0,2	++	0.35	++++				

Legend: —) no reaction; ±) a single scratching of the snout, and sneezing; +) repeated scratching of the snout and sneezing; + +) the same, with cough, instability; + + +) the same, with convulsions and incontinence of urine and feces; + + + +) the same, and death.

Note. The table does not include guinea pigs used for control of the toxicity of the preparation, nor also the control group of animals sensitized and desensitized with untreated tumor cells, since the former demonstrated that the doses used for the assaulting injection were nontoxic, and the latter gave no reaction to the assaulting injection in consequence of their complete desensitization with the untreated tumor tissue.

The viability of the irradiated cells was tested by intratesticular inoculation of rabbits.

The changes in the antigenic properties of the tumor cells under the influence of x-rays were studied by means of the anaphylaxis with desensitization reaction. Sensitization was carried out subcutaneously, and desensitization and the assaulting injection were given by intracardial injection. The interval between sensitization and desensitization was 22 days, and the interval between repeated intracardial injections was 2 hours.

In order to answer the question whether it was possible for the antigenic properties of the Brown-Pearce carcinoma cells to be changed under the influence of ionizing radiation, guinea pigs of the experimental group were sensitized by tissue of a Brown-Pearce tumor irradiated with 5000 r and densensitized by untreated carcinoma tissue. After testing for complete desensitization, as an assaulting injection we used tissue of a Brown-Pearce tumor irradiated with 5000 r. As a control of the experimental group we used guinea pigs sensitized and desensitized by unirradiated carcinoma tissue, and also guinea pigs on which the toxicity of the dose used for the assaulting injection was tested.

In Table 1 are given the results obtained in the first series of experiments.

As may be seen from the results in Table 1, the guinea pigs sensitized with irradiated tumor tissue could not be completely desensitized by untreated Brown-Pearce carcinoma tissue. All the guinea pigs reacted to the assaulting injection of irradiated tumor tissue by reactions from + to + + +.

Under the influence of irradiation with x-rays in vitro, changes therefore took place in the antigenic structure of Brown-Pearce carcinoma cells.

In order to answer the next question — whether the changes in the antigenic composition of the tumor cells depended on the dose of irradiation — 3 experimental groups of guinea pigs were used, which were sensitized with tumor tissue irradiated with 10,000 and 20,000 r, and desensitized with tissue irradiated with 2000 and 10 000 r.

After testing for completeness of desensitization, as assaulting injection we used tissue irradiated with the same dose of x-rays as that used for irradiating the tissues during sensitization. Thus, the first experimental

group of guinea pigs was sensitized with tissue irradiated with 10,000 r, and desensitized with tissue irradiated with 2000 r. As assaulting injection, tissue irradiated with 10,000 r was used. The second experimental group of guinea pigs was sensitized with tissue irradiated with 20,000 r and desensitized with tissue irradiated with 2000 r, and as assaulting injection, tissue irradiated with 20,000 r was used. The guinea pigs of the third experimental group were sensitized with tumor tissue also irradiated with 20,000 r, but were densitized with tissue

TABLE 2

Results of the Anaphylaxis with Desensitization Reaction with Antigens from Brown-Pearce Carcinoma Tissue Irradiated with Different Doses of X-Rays

Experimental group	Sensitization		Desensitization					Assaulting injection	
	antigen	dose	antigen	1st injection 0.2	2nd injection 0.35	3rd injection 0.5	4th injection 0.5	antigen	reaction
1	Brown-Pearce carcinoma tissue, irradiated with 10,000 r	0.5 0.5 0.5 0.5	Brown-Pearce carcinoma tissue, irradiated with 2000 r	++++ +++ ++ +++	++ — ++	+ — ±	— — —	Brown-Pearce carcinoma tissue, irradiated with 10,000 r	+++ ++ ++
2	Brown-Pearce carcinoma tissue, irradiated with 20,000 r	0.5 0.5 0.5 0.5		++ +++ + +++	++ ++ ++ —	+ — — —	— —	Brown-Pearce carcinoma tissue, irradiated with 20,000 r	+ +++ +++ +++
3		0.5 0.5 0.5 0.5	Brown-Pearce carcinoma tissue, irradiated with 10,000 r	++ +++ + +	+ ± — —	— — — —			± ++ ++ +

Legend as in Table 1.

Note. The table does not include the above-mentioned control groups of guinea pigs, since during sensitization and desensitization of the animals with tissue irradiated with the same dose of x-rays, complete desensitization of the guinea pigs was obtained, and injection of the animals with a suspension of tumor cells irradiated with 10,000 and 20,000 r as assaulting injection was found to be nontoxic.

irradiated with 10,000 r, and for the assaulting injection tissue was used which had been irradiated with 20,000 r.

As controls for the experimental group of animals in the second series of experiments, guinea pigs were used which had been sensitized and desensitized by tumor tissue irradiated with the same dose of x-rays, and also guinea pigs on which the toxicity of tumor cells irradiated with 10,000 and 20,000 r had been tested.

The results obtained in the second series of experimenta are shown in Table 2.

The above-mentioned control groups of guinea pigs are not included in Table 2, for in the course of sensitization and desensitization of the animals with tissue irradiated with the same dose of x-rays, complete desensitization of the guinea pigs was obtained, and injection of the animals with a suspension of tumor cells irradiated with 10,000 and 20,000 r as assaulting injection was found to be nontoxic.

It can be seen from the results in Table 2 that during sensitization of guinea pigs with tissue irradiated with 10,000 r complete desensitization did not take place when they were given injections of cells irradiated with 2000 r, just as in the case of sensitization of the animals with cells irradiated with 20,000 r, it was impossible to obtain complete desensitization by injecting tissue irradiated with 2000 r or 10,000 r.

Under these circumstances it must be pointed out that on the average the strength of the reaction of the guinea pigs to the assaulting injection was proportional to the dose of x-rays used for irradiation of the tissue in sensitization and desensitization.

As may be seen from the results in Table 2, the most pronounced reaction to the assaulting injection was observed in the guinea pigs of the second group, sensitized with tumor cells irradiated with 20,000 r, and desensitized with tissue exposed to the action of 2000 r.

We observed the least pronounced reaction in the guinea pigs of the third group, sensitized with a suspension of cells irradiated with 20,000 r and desensitized with similar material irradiated with 10,000 r.

Hence it followed that different doses of ionizing radiation clearly caused unidentical changes in the antigenic composition of the Brown-Pearce tumor.

The results obtained in the first and second series of experiments led to the conclusion that penetrating radiation, and in particular x-rays, cause a change in the antigenic composition of the Brown-Pearce carcinoma of rabbits.

These changes in the antigenic structure of the tumor tissue varied in relation to the dose of irradiation, and moreover the greater the difference between the doses of irradiation, the greater the change appeared in the antigenic structure of the irradiated tumor tissue.

SUMMARY

The work deals with the study of the effect of penetrating radiation (particularly of x-rays) on the antigenic structure of the Brown-Pearce carcinoma cells as well as with the establishment of a relationship between the irradiation doses and the changes in the antigenic structure of the tumor tissue.

The data obtained show that x-rays produce a change in the antigenic structure of the Brown-Pearce carcinoma. It varies depending on the irradiation dose (2000 r, 5000 r, 10,000 r and 20,000 r). The higher the irradiation dose the greater the changes of the antigenic structure of the irradiated tumor tissue.

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