MAST CELLS AND EOSINOPHILIC LEUKOCYTES IN THE FORMATION OF MAMMARY GLAND TUMORS IN FEMALE RATS IRRADIATED WITH γ RAYS AT THE AGE OF 4 WEEKS

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The onset of mammary gland tumors in female rats receiving a single dose of whole-body irradiation with γ rays in a dose of 200 R at the age of 4 weeks was studied. The first tumors were found in animals killed 6 months after irradiation, compared with at the 15th month after the beginning of the experiment in the control. All tumors found during the experiment in both irradiated and control rats were benign. Counting the mast cells and eosinophils in the mammary gland tissue showed a disturbance of the dynamics of the eosinophil content and a change in the mast-cell response during the course of radiation tumorigenesis.

KEY WORDS: *radiation; mammary gland tumors; mast cells; eosinophilic leukocytes.*

Mammary gland tumors are one special form of human radiation tumors [9, 10]. There is evidence in the literature of a high incidence of breast tumors in persons irradiated in early childhood [9]. The experimental study of this problem has so far been inadequate [8]. In the modern view mast cells belong to the cellular endocrine system of the body [6]. The number of mast cells and eosinophilic leukocytes reflects the functional activity of the connective tissue at the site of injury and in the region of tumor development [1-4, 5, 7]. According to observations by Zhuravleva and Antipova [4], the number of eosinophils in target tissues (uterus, mammary gland) is a morphological index of the presence of estrogenic hormones in these organs.

In this investigation the onset of mammary gland tumors in animals irradiated in the early periods of postnatal development was studied, with attention paid to the state of the tissue of the mammary gland at various stages of tumorigenesis using tests such as the number of mast cells and eosinophils.

EXPERIMENTAL METHOD

Altogether 127 noninbred female albino rats were used. At the age of 4 weeks 65 animals received a single dose of whole-body irradiation with ^{60}Co γ rays in a dose of 200 R at a dose rate of 232 R/min; 62 rats acted as the control. The animals chosen by random selection from the total population were killed by decapitation 3 and 6 h, 1, 7, 14, and 28 days, and 2, 3, 4, 6, 12, and 15 months after the beginning of the experiment. Mammary gland tissue with the regional lymph nodes was taken at the level of the mammary line from the left inguinal region, fixed in 10% neutral formalin solution, and embedded in paraffin wax. Sections 5-7 μ thick were stained with hematoxylin–eosin. The number of mast cells and of eosinophils was determined as the mean in 60 fields of vision under the magnification of 450×. The results were subjected to statistical analysis by Student's method with a level of significance of $P \leq 0.05$.

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TABLE 1. Frequency of Formation of Hyperplasia, Mastopathy, and Mammary Gland Tumors in Experimental and Control Rats

	Irradiation						Control					
Time of sacrifice, months	2	3	4	6	12	15	2	3	4	6	12	15
Total number of rats	4	9	3	10	6	10	4	9	8	8	6	8
with hyperplasia	0	1	0	8	5	3	0	0	0	6	1	2
with mastopathy	0	0	0	0	1	7	0	0	0	0	4	4
with benign tumors	0	0	0	1	2	4	0	0	0	0	0	2

EXPERIMENTAL RESULTS

The experimental results showed that irradiation accelerated the formation of mammary gland tumors (Table 1). After 6 months, a benign mammary gland tumor was found in 1 of the 10 irradiated females killed. Benign tumors were found after 12 and 15 months in 2 of the 6 and 4 of the 10 rats, respectively. In the control group benign tumors were found in 2 of the 8 animals killed at the 15th month of observation. The appearance of benign mammary gland tumors in the irradiated females was preceded by the development of hyperplasia, whereas tumors arose in the control rats after preliminary hyperplasia and also mastopathy (Table 1).

A study of the dynamics of the number of mast cells in the stroma of the mammary glands in the irradiated and control females during tumor formation showed that irradiation leads to a significant increase compared with the control in the number of mast cells in the mammary gland tissue on the 1st and 14th days and the 2nd, 6th, and 12th months (Fig. 1a). By the 14th day the accumulation of mast cells in the irradiated mammary gland reached a maximum. Their number then declined to reach the control level after 3-4 months. Between the 4th and 15th months of the experiment there was a further decrease in the number of mast cells in the mammary gland stroma. At these times, incidentally, their number was higher than in the control. A marked decrease in the number of mast cells coincided in time with the development of hyperplasia of the mammary gland epithelium of the irradiated rats (3rd month), and a further decrease in the number of these cells occurred up to the time of tumor development (6 months or later).

The number of eosinophils fell and remained low for 1 year. From the 12th and until the 15th month, i.e., until the time of appearance of tumors in the control rats, the number of eosinophils in the mammary gland tissue increased by 50%.

Irradiation changes the dynamics of the number of eosinophils in the mammary gland. In the irradiated rats an increase in the number of eosinophils to 8 times the initial level was found at the 3rd and 6th months of the experiment, with stabilization at these levels, 1.5% higher than the control, for 6-12 months of the experiment (Fig. 1b).

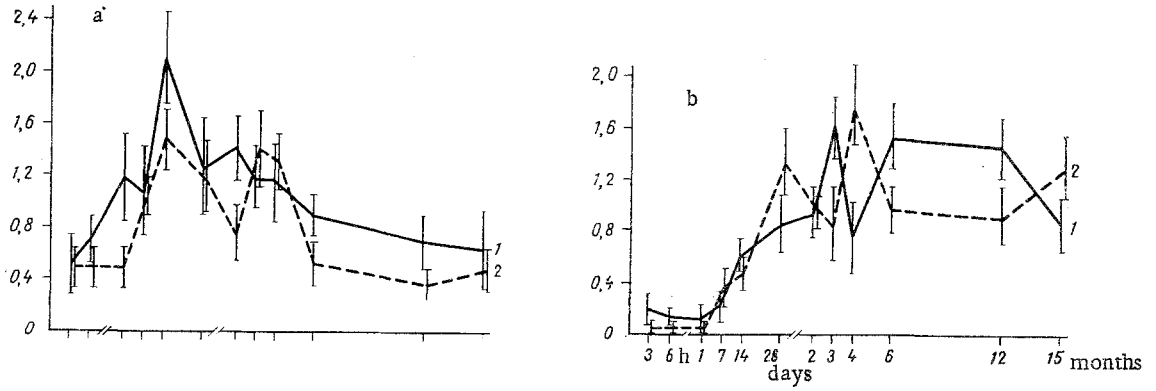

Fig. 1. Mast cells (a) and eosinophils (b) in mammary gland tissue of irradiated (1) and control (2) rats. Abscissa, time after irradiation; ordinate, number of cells in one field of vision.

Comparison of the dynamics of the numbers of mast cells and eosinophils in the mammary gland tissue of the unirradiated rats revealed a certain parallel in the change in their numbers. Irradiation disturbed this parallel by increasing the number of mast cells in the early stages and delaying the increase in the number of eosinophils at the same time. These differences in the response of the mast cells and eosinophils to irradiation were evidently due to the fact that these cells perform different functions in the mammary gland tissue. The content of eosinophils in the stroma of the mammary gland, as can be deduced from data in the literature [4], may perhaps reflect the presence of estrogenic hormones in them.

The results of these experiments thus showed that an important role in the genesis of radiation tumors of the mammary glands in rats receiving a single dose of irradiation in the early period of postnatal development is played by a disturbance of the dynamics of the number of eosinophils, which may probably be evidence of the accumulation of estrogenic hormones in the tissues of the mammary gland, and by a change in the response of the mast cells, as the cellular endocrine system of the body.

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ACTION OF CELL EXTRACT OF EHRLICH'S MOUSE ASCITES TUMOR ON MITOTIC ACTIVITY AND DNA SYNTHESIS IN THAT TUMOR

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An extract of cells of Ehrlich's ascites tumor inhibits the proliferative activity of its cells tissue specifically. The effect is expressed as a marked decrease in the number of dividing and DNA-synthesizing cells after injection of the extract. The mitotic index falls considerably as early as 2 h after the injection, reaches a minimum after 4-5 h, and returns to the control level again after 9-12 h. The radioactive index is on the whole uniformly low during the 18 h of the experiment.

KEY WORDS: *chalone; Erhlich's ascites tumor; mitotic index; index of labeled nuclei.*

Starting in 1964 [2], considerable attention has been paid to the study of tissue-specific inhibitors of cell division, or chalones. An essential factor in these investigations

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