

ROLE OF THE DIRECT ACTION OF RADIATION
IN THE MECHANISM OF DEVELOPMENT OF MAMMARY
GLAND TUMORS

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UDC 618.19-006-092:617-001.29

The role of the direct action of radiation in the genesis of mammary gland tumors in animals of both sexes was studied in experiments on noninbred albino rats. In two series of experiments the anterior or posterior half of the rat's body was irradiated with x rays in doses of 200 to 1000 rad. Tumors of the mammary glands appeared considerably earlier and were more numerous in the irradiated parts of the body of both females and males than in the unirradiated glands or in control animals. Females developed mammary gland tumors after exposure to smaller doses and in a higher proportion of cases than males.

Investigations have shown that after whole-body irradiation with various types of ionizing radiation animals develop benign and malignant tumors of the mammary glands [1-6]. An essential role in the genesis of these tumors is played by indirect factors, notably a disturbance of correlations within the system: pituitary → ovaries → mammary glands [1-3]. In their analysis of the mechanisms of tumor development, investigators frequently forget that during whole-body irradiation the mammary glands are also themselves exposed to the action of the rays. The question naturally arises of the role of the direct action of radiation in the mechanism of development of mammary gland tumors. Little attention has so far been paid to this aspect of the problem [4, 5, 7].

It was therefore decided to study the role of the direct action of radiation in the genesis of mammary gland tumors.

EXPERIMENTAL METHOD

Experiments were carried out on 460 noninbred albino rats of both sexes. The age of the rats at the time of the experiment was 3-4 months; females weighed 150-170 g and males 180-200 g. In the experiments of series I on 151 female rats the anterior half of the body was irradiated, while in series II, on 233 rats of both sexes (130 females and 103 males), the posterior half of the body was irradiated. The control group consisted of 76 rats (51 females and 25 males).

The rats were irradiated with x rays on the RUM-3 apparatus at a distance of 50 cm from the tube. The dose rate was 22 R/min. During irradiation the unirradiated part of the body was protected with a lead screen (5 mm). The doses used were 200, 400, 600, 800, and 1000 rad. From 15 to 32 rats were used for each dose.

The localization, frequency, and rate of development of the mammary gland tumors in the irradiated and unirradiated parts of the body and also in the control rats were determined by palpation and visual observation on the animals at the different times of the experiment. The frequency of tumor development was expressed as a percentage.

Institute of Biophysics, Ministry of Health of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 75, No. 5, pp. 68-70, May, 1973. Original article submitted June 19, 1972.

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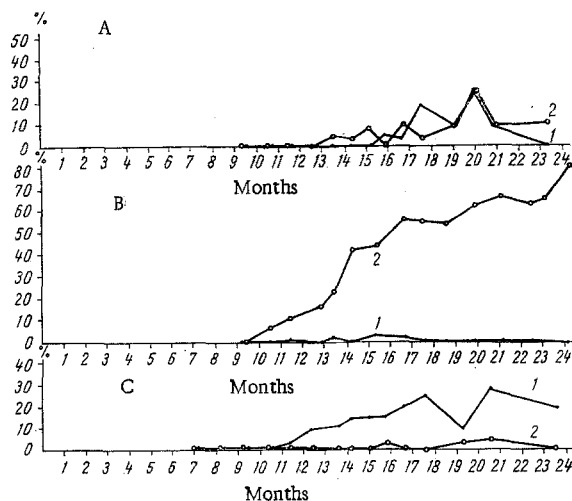


Fig. 1. Frequency of development of mammary gland tumors in rats in anterior (1) and posterior (2) halves of the body at various times and under different conditions of irradiation: A) control; B, C) irradiation of posterior and anterior half of body, respectively. Abscissa, time of observation (in months); ordinate, frequency of tumor development (in %).

a maximum in the irradiated anterior half of the body after 17.6 and 20.6 months, when it was 25% (in 14 of 56 rats) and 28.6% (in six of 21 rats), respectively. At these same times the frequency of mammary gland tumors in the unirradiated posterior half of the body was 0 and 4.7% (in one of 21 rats). In the control animals the incidence of mammary gland tumors at these times was 18.5% (in five of 27 rats) and 9.1% (in two of 22 rats), respectively, in the anterior half of the body and 3.7% (in one of 27 rats) and 9.1% (in two of 22 rats), respectively, in the posterior half.

In the experiments of series II the effect of irradiation of the posterior half of the body of females and males on the incidence and localization of mammary gland tumors was studied. Just as in the experiments in which the anterior half of the body was irradiated, tumors appeared earlier in the irradiated half of the body. With doses of 200–1000 rad the first mammary gland tumors in females (in seven of 105 rats) in the irradiated half of the body were found after 10.5 months. At this time no tumors were present in the unirradiated half of the body or in the control rats. In one of 103 female rats (0.97%) a tumor was found in the unirradiated half of the body after 11.4 months. The frequency of tumor development in the irradiated half of the body at this time was 10.7% (in eleven of 103 rats); no tumors were present in the control animals at this time. The frequency of development of mammary gland tumors 15.4 months after irradiation was 46.4% (in thirty-two of 69 rats) in the irradiated half of the body in females and 2.9% (in two rats) in the unirradiated half. The maximal frequency of development of mammary gland tumors in the females in the irradiated half of the body was observed after 20 months when they were found in 63% of rats (in seventeen of 27 animals), but none were present in the unirradiated half. The frequency of tumor development in the anterior and posterior halves of the body was the same in the control unirradiated rats, namely 25% (in two of eight rats).

Unlike in females, mammary gland tumors develop spontaneously in males only rarely. In the control males the first mammary gland tumor was found 21 months after the beginning of the experiment (in one of 13 rats, 7.7%), and in the control females after 13.5 months (in two of 42 rats, 4.8%). In males after irradiation of the posterior half of the body in doses of 400–800 rad the first mammary gland tumors were found in 13.3 months (in two of 52 males or 3.8%), i.e., almost 8 months earlier than in the control.

Throughout the period of observation (23 months) mammary gland tumors in males were always found in the irradiated half of the body. After 16.7 months the frequency of development of mammary gland tumors

EXPERIMENTAL RESULTS AND DISCUSSION

Mammary gland tumors developed in both irradiated and control rats. However, the times of appearance, frequency, and localization of the neoplasms differed significantly. In the control animals mammary gland tumors appeared considerably later and in a smaller percentage of cases than in the irradiated animals. The frequency of mammary gland tumors in the anterior and posterior halves of the body was approximately the same in the control rats but in the irradiated animals tumors developed almost entirely in the irradiated glands (Fig. 1).

For instance, after irradiation of the anterior half of the body in doses of between 200 and 1000 rad the first mammary gland tumors in the irradiated half of the body were found in 11.4 months (in three of 103 rats or 2.9%), whereas in the unirradiated half of the body they were found in 15.8 months (in two of 59 rats or 3.4%). In the irradiated half of the body the frequency of tumor development at this time was 15.3% (in nine of 59 rats). The first mammary gland tumors in the anterior half of the body of the control rats (in one of 21 rats or 4.7%) were found after 15.8 months, and in the posterior half of the body after 16.6 months (in three of 31 rats or 9.7%). The incidence of mammary gland tumor development reached

in the irradiated males was 10% (in three of 30 rats). The frequency of tumor development in males in the irradiated posterior half of the body throughout the experiment was considerably lower than in females. For example, after 16.7 months the frequency of development of mammary gland tumors in males was 10% and in females 56.6% (in thirty-four of 60 rats), while after 21 months it was 30% (in three of 10 rats) and 67% (in twelve of 18 rats), respectively.

In females an increase in the incidence of mammary gland tumors in the irradiated half of the body was observed whatever the dose used, including after irradiation in doses of 200 and 400 rad. No mammary gland tumors developed in 22 males irradiated in a dose of 400 rad. They were observed only in males irradiated in doses of 600 and 800 rad.

Mammary gland tumors thus arise in females (whether spontaneously or under the influence of ionizing radiation) much more often than in males. In irradiated females mammary gland tumors arise earlier, in a higher percentage of cases, and after exposure to smaller doses than in males. Both in males and in females the direct action of ionizing radiation plays a very important role in the genesis of neoplastic transformation of the mammary gland cells. These results correlate well with the observations of Bond et al. and of other workers [4, 7] who also draw attention to the important role of the direct action of radiation in the genesis of mammary gland tumors.

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