MECHANISM OF REGRESSION OF MAMMARY GLAND CARCINOMA IN LACTATING RATS

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Regression of transplantable mammary gland carcinoma in rats was shown to depend on the intensity of lactation (the number of young in the litter). This suggests a link between regression of mammary gland carcinoma and the action of endogenous prolactin, the secretion of which is increased during normal lactation.

It has often been reported in the literature that spontaneous regression of spontaneous, induced, and transplanted mammary gland carcinoma can take place in lactating mice and rats [8, 11, 13-15]. These observations do not agree with the widespread view that lactation, like pregnancy, stimulates the growth of mammary gland carcinoma [1, 6, 7]. They are also contrary to the view that prolactin, as the pituitary hormone promoting lactation, stimulates the development and growth of mammary gland carcinoma [16-19, 21].

At the same time, these observations agree fully with the marked antitumor action of bovine prolactin on transplanted mammary gland carcinoma of rats and spontaneous mammary gland tumors of mice, established in the writers' laboratory [2, 3, 5, 9], and also with the results of investigations indicating that elevation of the endogenous prolactin level in the body prevents the development of mammary gland tumors induced by estrogens and chemical carcinogens [10]. In the light of these facts, it can be assumed that regression of mammary gland carcinoma in the period of lactation takes place because the production of endogenous prolactin is sharply increased under these circumstances.

To shed light on this problem, regression of mammary gland carcinoma was studied in animals with a varied intensity of lactation. The intensity of lactation in rats and the number of young in the litter determine the level of secretion of endogenous prolactin by the pituitary [20, 22]. Consequently, the intensity of lactation, which was regulated by varying the number of young in the litter, can be used to judge the level of secretion of endogenous prolactin. If the writers' hypothesis regarding the mechanism of regression of mammary gland carcinoma in lactating animals is correct, normal lactation, when prolactin production is increased, must lead to regression of the tumor, while absence of lactation, when no prolactin is formed in the pituitary, would not cause regression of mammary gland carcinoma.

EXPERIMENTAL METHOD

Experiments were carried out on a transplantable mammary gland carcinoma of rats (RMK-1), the experimental model of a tumor reactive to hormonal influences [4]. The tumors were transplanted into noninbred pregnant rats at the end of pregnancy, 1-5 days before parturition, usually on the day when the animals were brought from the nursery of the Academy of Medical Sciences of the USSR. Several analogous experiments were performed and the results of one of them are described below.

Observations were made on 30 pregnant rats divided into 3 groups. Group 1 included nonlactating rats which had themselves refused to feed their young 1-3 days after birth; group 2 included poorly lactating rats, each feeding from 2 to 4 young animals (on the 5th-7th day of lactation the number of rats in the litter

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TABLE 1. Relationship between Regression of Transplanted Mammary Gland Carcinoma of Rats (RMK-1) and Intensity of Lactation

Group of rats	Number of rats in litter	Absorption of tumors (after 25-40 days)	
		absolute[1]	%
1-(Not lactating after parturition)	–	0/7	0
2-(Lactating weakly)	2-4	2/10	20
3-(Lactating normally)	7-9	6/13	53

[1]Numerator gives number of rats with absorbed tumors; denominator total number of rats with tumors.

was reduced). Group 3 included normally lactating rats, feeding at least 7-9 young in the litter (some workers consider that the prolactin output in rats and mice during lactation is highest if the litter contains at least 4 young, while others consider that the number is at least 6 [12, 20]).

The experiment continued for 40 days, starting from the day of transplantation of the tumor. In the course of the experiment, the tumors were measured every 4-5 days by the method usually adopted in experimental tumor chemotherapy, and the number of animals with regressed tumors was counted.

EXPERIMENTAL RESULTS

The results for regression of mammary gland carcinoma in the rats in relation to the intensity of lactation are given in Table 1. They show that in the rats of group 1, not lactating after birth, regression of the tumor was not observed in any of the 7 animals. All the animals of this group died from tumors during the experiment. In group 2, consisting of weakly lactating rats feeding not more than 2-4 young in the litter, the tumors began to diminish in size on the 15th and 19th days of lactation in 2 of the 10 rats (20%), and they subsequently underwent complete absorption. All the remaining animals likewise died from tumors during the experiment. In the rats of group 3 with normal lactation, feeding at least 7-9 young in the litter, by the end of the period of lactation (on the 18th-22nd day) the tumors in 6 of the 13 animals (53%) which had hitherto been growing began to decrease in size, and they were completely absorbed in the course of the experiment, whereas the remaining animals died from tumors. [Incidentally, spontaneous absorption of tumors of strain RMK-1 is observed in not more than 10-15% of animals.]

These results thus showed that regression of mammary gland carcinoma occurred only in normally lactating animals, and it was virtually absent in weakly lactating animals or animals not lactating at all after parturition. Since regression of mammary gland carcinoma was dependent on the normality of lactation, when secretion of endogenous prolactin by the pituitary is greatest, there are grounds for linking regression of mammary gland carcinoma with the action of endogenous prolactin. The spontaneous regression of mammary gland carcinoma observed in normally lactating animals suggests that lactation may have a therapeutic action on mammary gland carcinoma.

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