EFFECT OF OVARIECTOMY ON LIFE SPAN AND INCIDENCE OF MAMMARY GLAND TUMORS IN IRRADIATED RATS

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Among the various pathological effects of radiation, in recent years much attention has been paid to its carcinogenic action, in the genesis of which hormonal disturbances, besides the direct action of the rediation, play an important role. As a result, tumors of various types may arise in the glands of internal secretion, including neoplasms of the pituitary, ovaries, adrenals, thyroid, reproductive organs, and also the mammary glands [2, 3].

There is a close connection between the functional state of the ovaries and the appearance of mammary gland tumors. Ovariectomy considerably lowers the incidence of both spontaneous tumors and tumors induced by ionizing radiation in the mammary glands of female mice and rats of different lines [1, 5].

In the present investigation the effect of ovariectomy on the frequency and the speed of appearance of mammary gland tumors and their dependence on the time relationships between irradiation and ovariectomy were studied, and the effect of removal of the ovaries on the life span of the experimental animals was also examined.

EXPERIMENTAL METHOD

Experiments were carried out on 137 female Wistar rats initially weighing 110-115 g at the age of 3 months. The animals were divided into four groups. The rats (48) of group 1 were the control. The animals of groups 2 (27), group 3 (32), and group 4 (30) were irradiated with γ-rays from Co^{60} (dose 300 R, dose rate 245 R/min). The rats of group 2 were only irradiated, those of group 3 underwent ovariectomy 6 days before irradiation, and the rats of group 4 had their ovaries removed 64 days after irradiation. The results of preliminary experiments showed that a dose of 300 R causes mammary gland tumors to develop in a high proprtion of rats. Throughout the experiment, which lasted for 30 months, the rats were inspected and palpated once a month. As a result of these investigations the incidence and the time of appearance of the mammary gland tumors in the experimental animals could be assessed. Rats which died were autopsied and the character and type of the tumor were determined from the results of morphological investigation.

EXPERIMENTAL RESULTS

Ovariectomy very materially affected the mortality rate and the mean life span of the irradiated rats (Fig. 1).

It is clear from Fig. 1 that the castrated irradiated rats died more slowly than the intact irradiated animals. The differences in the mortality rate were most clearly seen in the late stages of the experiment (after 15-18 months), when mammary gland tumors developed intensively in the rats.

The mean life span of the irradiated rats was 17.5 months, compared with 22.2 and 21.4 months in the animals ovariectomized before and after irradiation respectively, and 24 months in the controls. At the time when 50% of the ovariectomized animals had died, only 10% of the intact irradiated rats were still alive. By the 23rd month all the irradiated rats had died, and at this time, among the animals ovariectomized before and after irradiation, only 60 and 64% respectively had died.

The slower mortality among the ovariectomized rats in the late periods (after 20 months or more) was was statistically significant. For the 20th and 22nd months after irradiation, χ^2 was between 4 and 13,

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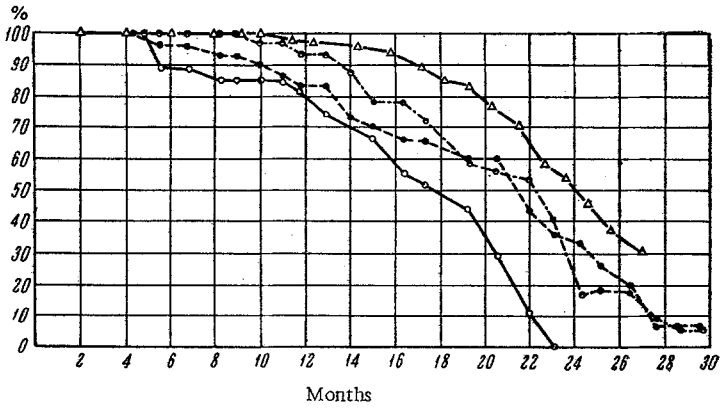

Fig. 1. Effect of castration and irradiation with γ-rays from Co^{60} in a dose of 300 R on the mortality rate among rats. Triangles – control; white circles – irradiation; half-black circles – castration + irradiation; black circles – irradiation + castration.

and the value of P correspondingly was 0.04-0.001. In the earlier stages (before 18 months) the differences between the mortality rates of these two groups of animals were not significant. After 17.6 months, for instance, $\chi^2_{[1]} = 2$, and $P = 0.15$.

The observations on the experimental animals showed that irradiation and ovariectomy had a considerable influence on the incidence and the time of appearance of mammary gland tumors in the rats. In the intact irradiated rats mammary gland tumors appeared much earlier than in the control animals (Fig. 2).

Tumors were found in the irradiated rats 8 months after irradiation, compared with 14 months after the beginning of the experiment in the controls. In the irradiated animals, not only did the tumors appear sooner, but their total incidence was greater. The maximal incidence of tumors in the irradiated animals (in 78.5% after 17 months) also was higher in the early periods than in the control rats (in 53.5% after 27 months).

Regardless of whether it was carried out before or 64 days after irradiation, ovariectomy considerably delayed the appearance and lowered the incidence of the mammary gland tumors (Fig. 2). As mentioned above, in the irradiated rats mammary gland tumors appeared 8 months after, and in the castrated rats 14 months after irradiation. The maximal incidence of mammary gland tumors, which reached 17-22% in the ovariectomized animals, was much lower than in the intact irradiated animals (78.5 and 100% 17 and 22 months after irradiation).

Statistical analysis of the results by means of the χ^2 criterion showed that the differences between the incidence of mammary gland tumors in the intact and castrated irradiated rats were significant ($P = 0.015$-0.001).

No significant differences in the incidence of mammary gland tumors were found in the animals castrated before and 64 days after irradiation. The incidence of mammary gland tumors 15, 17, and 20 months after irradiation in the animals castrated before irradiation was 12, 13, and 22% respectively, compared with 9.5, 10, and 16.7% in the animals castrated 64 days after irradiation.

The castrated irradiated animals developed mammary gland tumors 2-3 months earlier (after 14-15 months) than the controls (after 17 months) which were not irradiated. These differences are significant ($\chi^2_{[1]} = 3.9 - 7.8$; $P = 0.05 - 0.005$). In the later periods (after 24 months) the incidence of tumors was slightly higher in the control animals (see Fig. 2). However, these differences are not significant ($\chi^2_{[1]} = 0.6 - 3.2$; $P = 0.3$-0.07).

The appearance of mammary gland tumors in some of the castrated animals may be regarded as evidence that the other endocrine glands are concerned in the genesis of neoplasms of this type. The conclusion is also supported by the observation [1] that in such cases the development of the tumor is frequently associated with hyperplasia and a tumor of the adrenal cortex, which in the opinion of the author cited may lead to the development of fibroadenomas of the mammary glands.

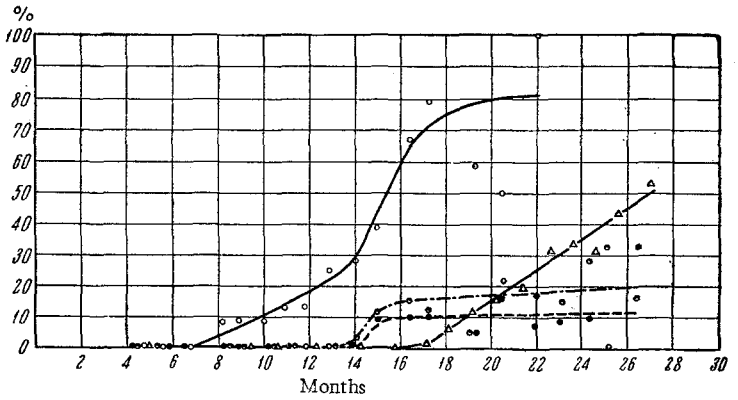

Fig. 2. Effect of castration on the incidence and time of appearance of mammary gland tumors in rats irradiated with γ-rays from Co^{60}. Legend as in Fig. 1.

Some of the animals which died were autopsied and the results of the pathological examination revealed not only a much lower incidence of mammary gland tumors in the ovariectomized rats (in 80% of the irradiated rats, in 18.7% of those castrated before and 8.3% castrated after irradiation), but also a higher incidence of hyperplasia and neoplasms of the adrenals, leukemia (in 4 of the 28 rats ovariectomized before and after irradiation, but in none of the 10 intact, irradiated animals), and gross adiposity (in 10 of the 28 rats), which was not observed in the intact irradiated rats. These figures concerning the effect of castration on the incidence of leukemia in irradiated rats are of course to few to allow a final conclusion to be drawn on this question. However, they are in good agreement with results reported by other workers [4, 6], who observed that castration stimulates the development of leukemia in irradiated animals. This fact shows that it is not only the direct action of radiation on the hemopoietic organs, but also indirect factors, including hormonal distrubances developing in the irradiated organism which play an important role in the genesis of the leukemias, as also of mammary gland tumors. They also show that the same supplementary action may differ in its influence on the manifestation of different reactions of the body to irradiation.

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