HISTOLOGICAL CHANGES IN THE OVARY AFTER LOCAL IRRADIATION

A. V. Gubareva

UDC 618.11-001.29-091

Local x-ray irradiation of one ovary in a dose of 150 R, with the whole of the rest of the body including the other ovary screened, was not followed by a statistically significant increase in the frequency of ovarian tumors. However, the latent period of development of tumors in the screened ovary was shortened by a statistically significant margin compared with the latent period of development of tumors in the ovaries of mice subjected to no procedure and acting as control.

* * *

The pathogenesis of ovarian tumors induced by irradiation is based on disturbance of pituitary–gonad relationships. However, the role of mutations, inevitably arising in the ovarian cells following exposure to ionizing radiation, has not yet been adequately explained. The view that these changes are not of decisive importance in the development of tumors in irradiated ovaries [2, 3] requires clarification.

The object of this investigation was to examine the role of structural changes in the ovary resulting from the direct influence of irradiation in the onset and development of ovarian tumors.

To determine the importance of primary radiation injury of the ovaries in the development of neoplasms, conditions of irradiation must be chosen which cause least disturbance to the state of the body. Such conditions can be provided, it is considered, by local irradiation of one ovary, with the whole of the rest of the body including the other ovary screened. The lost function of one ovary will then be compensated by the other.

It has previously been shown [1] that the changes taking place in the ovaries of mice irradiated with a dose of ionizing radiation (whole-body γ-ray irradiation in a dose of 200 R) producing castration take place in a series of stages: diffuse hyperplasia–nodular proliferation–tumor. The development of compensatory and hyperplastic changes in the ovaries following irradiation has been observed one month after irradiation while the largest number of tumors (63.1 ± 4.9%) has been observed to appear by the 18th month.

EXPERIMENTAL METHOD

Experiments were carried out on 407 noninbred virgin female albino rats of the "Rappolovo" breed, weighing 18–20 g. The animals were divided into three groups: group 1, 147 mice with local irradiation of the right ovary; group 2, 25 unirradiated mice, subjected to all manipulation necessary for local irradiation of the ovary apart from irradiation itself; group 3, 235 mice subjected to no procedure whatever (control).

The right ovary was irradiated in a single dose of 150 R on the RUM-11 apparatus under the following conditions: voltage 180 kV, current 17 mA, filters 0.5 Cu+1.0 Al, dose rate 77 R/min. During irradiation the mouse, which was anesthetized with nembutal, was placed in a lead box with walls 0.7 cm thick, and the right ovary was drawn outside the box through a hole in the side wall by means of a ligature attached to the uterine cornu. The exteriorized ovary was placed on a miniature waxed wooden table on which it was irradiated.

Most of the mice were left until natural death, but a few animals of each group were sacrificed in small batches at intervals of 2 weeks (to study early changes in both the irradiated and the unirradiated ovaries).

Laboratory of Radiation Genetics and Late Radiation Pathology, Central Roetgeno-Radiologic Research Institute, Ministry of Health of the USSR, Leningrad (Presented by Academician of the AMN SSSR D. A. Biryukov [Deceased]). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 5, pp. 61-63, May, 1969. Original article submitted July 1, 1968.

Fig. 1. Irradiated right ovary 1.5 months after x-ray irradiation: ovary small, abundance of follicles without oöcytes on surface, 120 ×.

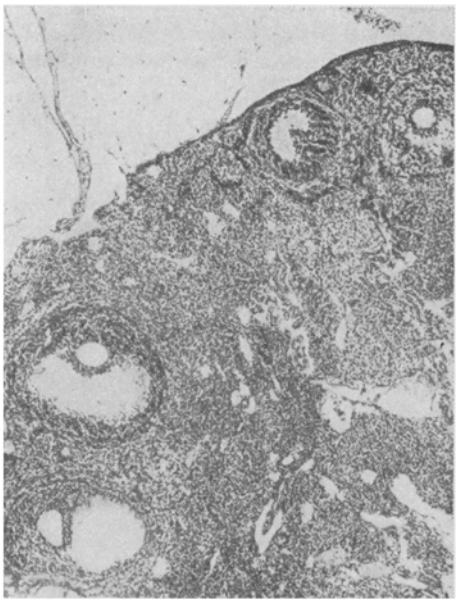

Fig. 2. Screened functioning ovary of the same mouse as in Fig. 1, 120 ×.

The ovaries were embedded in paraffin wax and series of histological sections were studied.

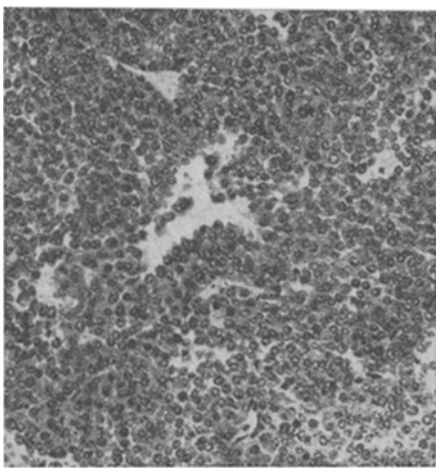

Fig. 3. Granulosa-cell tumor of irradiated ovary, 260 ×.

EXPERIMENTAL RESULTS

Histological examination of locally irradiated ovaries one month after irradiation in a dose of 150 R revealed a picture of complete and irreversible sterilization of the gland (Figs. 1 and 2). The ovaries did not contain ripe or ripening follicles, but only structures resembling primordial follicles, but without oöcytes. The theca tissue (the specific interstitial tissue of the ovarian cortex) was atrophic. This state of the ovary was observed for 16 months after irradiation. Not until the end of this period was the development of hyperplastic changes observed in the irradiated ovaries of 22 of the 102 mice (21.5 ± 4%), indicating the development of a dyshormonal state in the aging animals. However, the degree of severity and the extent of these changes were very slight.

The dyshormonal state was also reflected in the structure of the unirradiated ovaries of the experimental and control old mice. A study of the histological structure of the unirradiated ovaries of the mice, for instance, revealed two distinct forms of age involution: simple (typical) and complex (atypical). Whereas in the first case involution took the form of simple shrinking of specific structures and atrophy of the ovary, in the second case loss of the specific functioning elements was accompanied by the appearance of foci of hyperplastic type. Atypical involution of this type in the screened ovaries of locally irradiated mice was observed in 17 of 104 mice (16.3 ± 3.6%). Senile involution of the screened ovaries began at an earlier period than in the ovaries of mice not subjected to any procedure.

Tumors were found in the irradiated ovaries of 10 of 69 mice (14.5±2%) surviving until the day of death of the first animal with a tumor of the irradiated ovary. Neoplasms were found in the screened ovaries of 9 of the 104 mice (8.6 ± 2.7%). The absence of statistically significant differences in the frequency of development of neoplasms ($t = 1.2$) in the irradiated and screened ovaries of the experimental mice suggests

that probably somatic mutations do not play an essential role in the genesis of ovarian tumors following irradiation. However, it is considered that this conclusion is nothing more than conjectural in character, because the disturbance of feedbacks in the pituitary–gonads system required for the operation of radiation mutation takes place, as our investigations showed, 16 months later than in totally irradiated animals, and only in a few of the mice undergoing local irradiation of one ovary. The difference between the mean life spans of these two groups of animals is only 4 months, however (601.9 ± 13.9 days with local and 483.9 ± 24 days with whole-body irradiation).

The number of tumors in the ovaries (17.8 ± 7.3%) of control mice not subjected to any procedure and with a mean life span of 594.6 ± 26.4 days was indistinguishable from the number of tumors developing in the screened ovaries of the locally irradiated mice ($t = 1.2$). However, the latent period of development of the tumors in the screened ovaries was shortened by a statistically significant degree ($t = 3.6$).

Neoplasms in the irradiated ovaries were mixed in structure in 7 cases out of 10, consisting of a combination of tubular structures with granulosa cells, varying in their degree of saturation with lipids (Fig. 3). In the screened ovaries only granulosa-cell tumors were found, and they frequently were multicentric, arising both from atretic and atypically developing follicles. Only once in the control group of mice was a tubularadenoma of the ovary found, and all the other neoplasms were of the granulosa-cell type.

LITERATURE CITED

1. A. V. Gubareva, Med. Radiol., No. 4, 37 (1968).
2. M. H. Li, W. U. Gardner, and H. S. Kaplan, J. Nat. Cancer Inst., 8, 91 (1947).
3. L. Lick, A. Kirschbaum, and H. Mixer, Cancer Res., 9, 532 (1946).