MORPHOLOGY AND FUNCTION OF THE ADENOHYPOPHYSIS IN LETHALLY IRRADIATED RECIPIENTS AFTER BONE MARROW TRANSPLANTATION

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The writers previously described [8, 9] that, besides changes in functions of organs of the lymphomyeloid complex in lethally irradiated animals the histologic structure and functional activity of endocrine organs such as the adrenals and pancreas also were disturbed. Transplantation of syngeneic bone marrow helped to restore the normal histologic structure of the above organs, and a definite time course of restoration of their function was observed.

Considering the leading role of the pituitary gland in regulation of function of the endocrine organs, and also the lack of information about its morphology and functional state in lethally irradiated recipients protected by bone marrow, the aim of the present investigation was to study changes in the time course of the morphologic and functional state of the pituitary gland in lethally irradiated recipients at different stages after transplantation of bone marrow cells.

EXPERIMENTAL METHOD

Experiments were carried out on 120 inbred female (CBA × C57BL)F_1 mice aged 2 months. The animals were divided into three groups: 1) control group (intact mice), 2) lethally irradiated mice, and 3) lethally irradiated mice receiving syngeneic bone marrow.

Irradiation was given on the RUM-17 apparatus. The conditions of irradiation were: dose rate 39.5 R/min, 200 kV, 10 μA. Bone marrow was taken from the femora of the mice and injected intravenously in a dose of $1 \cdot 10^7$ cells/ml. Irradiation of the animals and transplantation of hematopoietic cells were carried out at the same time, in the fall and winter and between 10 a.m. and noon. The state of the pituitary gland was studied 1, 3, 7, 10, 20, 40, and 90 days after irradiation and transplantation of bone marrow. Three mice from the experimental and control groups were taken at each time. After decapitation the pituitary was removed and fixed in neutral formalin. Paraffin sections 6-7 μ thick were stained with hematoxylin and eosin and by Mallory's method.

The anterior lobe of the pituitary was studied. Its state was assessed by investigation of its histologic structure and by counting the number of cells of the chromophilic and chromophobic series in a horizontal section passing through all three lobes, in which the area of the anterior lobe of the pituitary was maximal. The relative percentages of the cells were calculated, the area of the cells and their nuclei measured by means of an ocular micrometer, and the nucleoplasmic ratio in these groups of cells was determined.

To determine the character of the functional state of adenohypophyseoadrenocortical system in the lethally irradiated recipients, the blood serum corticosterone level was determined at different times after irradiation and bone marrow transplantation by radioimmunoassay.

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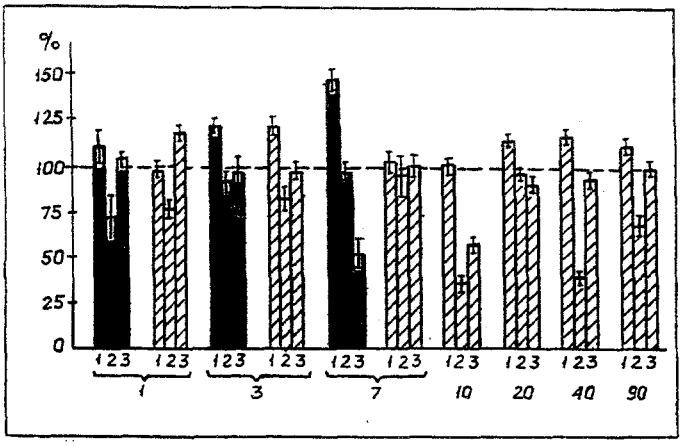

Fig. 1. Changes in cell composition in anterior lobe of pituitary of lethally irradiated mice after bone marrow transplantation. Black shading – irradiation, oblique shading – irradiation + bone marrow transplantation. Control (intact animals) taken as 100%. 1) Acidophilic, 2) basophilic, 3) chromophobic cells. Abscissa, days after irradiation.

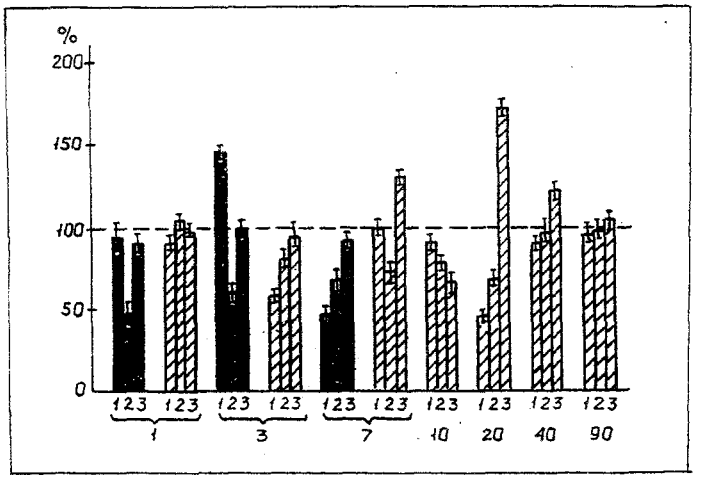

Fig. 2. Changes in nucleoplasmic ratio in secretory cells of anterior pituitary of lethally irradiated mice after bone marrow transplantation. Legend as to Fig. 1.

The results were subjected to statistical analysis by the Fisher–Student method.

EXPERIMENTAL RESULTS

In histologic sections stained with hematoxylin and eosin the anterior lobe of the pituitary of the control animals (group 1) consisted of widely branching cellular bands. Capillaries, moderately filled with blood cells, could be seen among them.

Groups of chromophobic and chromophilic cells were identified. The chromophobic cells contained small, basophilically stained nuclei, surrounded by a narrow border of pale lilac cytoplasm. The basophilic cells were polymorphic, much larger than the chromophobic cells, oval and irregular in shape, with eccentrically situated violet nuclei and with pale lilac cytoplasm.

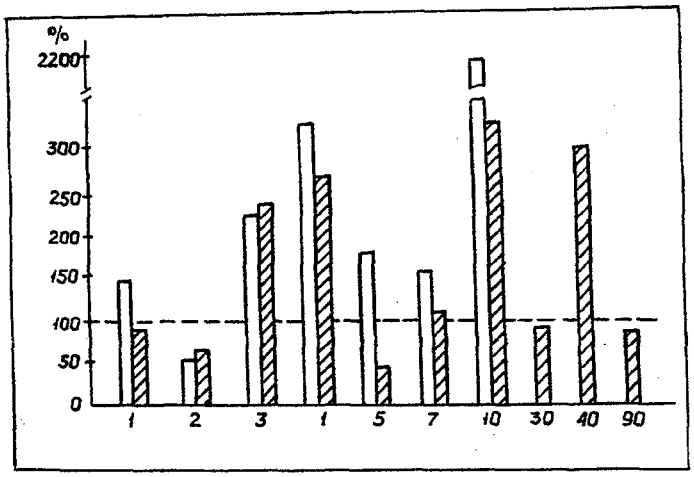

Fig. 3. Changes in time course of blood corticosterone level of lethally irradiated mice, protected and not protected with bone marrow. Unshaded columns – irradiation, shaded – irradiation + bone marrow transplantation. Control (intact animals) taken as 100%. Abscissa, days after irradiation.

The acidophilic cells occupied an intermediate position for size between chromophobic and basophilic cells. They were oval in shape, with a centrally located delicately reticular nucleus and pink cytoplasm.

Counting the number of secretory cells showed that in the control animals acidophils accounted for 54 ± 2.33%, basophils for 7.5 ± 0.29%, and chromophobes for 38.5 ± 3.12% (Fig. 1).

In the animals of group 2 histologic changes in the tissues of the anterior pituitary were observed starting with the 1st day after irradiation. The number of secretory cells with pycnotic nuclei and vacuolation of the cytoplasm was increased, and most cells were small in size and the blood vessels dilated and congested with blood. At the time of the animals' death dystrophic changes had progressed in the secretory cells, most of which were destroyed and replaced by cellular debris; fluctuation of the number of secretory cells was observed, due to an increase in the number of acidophils and a decrease in the number of basophils and chromophobes, most marked on the 7th day after irradiation (76 ± 4.32% of acidophils, 6 ± 0.51% of basophils, 18 ± 0.27% of chromophobes).

An increase in the number of acidophilic cells in mammals, taking place after whole-body irradiation with large doses of x-rays has been noted in the literature [2, 4]. As will be clear from Fig. 2, the nucleoplasmic ratio in acidophils and chromophobes during the 1st day after irradiation was close to the control value, whereas that of the basophils was sharply reduced. On the 3rd day this ratio in the acidophils was increased by almost 1.5 times compared with the control, whereas in basophils and chromophobes it remained at its previous level. After 7 days, near the time of death of the animals, the nucleoplasmic ratio fell in the acidophils, whereas in the basophils and chromophobes it remained at a lower level than in the control series. Since changes in the functional state of the organs are reflected in the dimensions of cell nuclei [7], the results are evidence of fluctuations of adenohypophyseal functional activity in lethally irradiated animals.

Some workers [1, 5, 6] consider that in the first 3 days after lethal irradiation of animals there is a transient increase in functional activity of the gland, as a result of which pituitary hormones stimulating activity of other endocrine organs, especially the adrenals, are released into the blood; this is evidently a manifestation of defensive reactions of the body to irradiation.

This conclusion is confirmed by results described in a previous communication [8], in which an increase in mass of the adrenals was observed, together with widening of the adrenal cortex on account of the zona fasiculata and zona reticularis, and also by the results of determination of the serum corticosterone level in lethally irradiated animals. For instance, the serum corticosterone level of the irradiated animals after 1, 3, and 7 days was higher than in the control and indicated enhanced secretory function of the adrenals at these times (Fig. 3).

In the animals of group 3, 24 h after irradiation and bone marrow transplantation the histologic structure of the tissue of the anterior lobe of the pituitary was comparable with that in animals of the control group, but there was a tendency for the number of acidophils and basophils to fall and for the number of chromophobes to rise. After 3 days changes were observed in the adenohypophysis, in the form of dilatation of sinuses, which were filled with blood, and the nuclei of some cells were hyperchromic and lenticular in shape. Some cells had pycnotic nuclei. The number of acidophilic cells was increased, the number of chromophobes was reduced, and remained so throughout the period of observation (until 90 days), whereas the number of basophils varied from minimal (2 and 2.2% after 10 and 40 days respectively) to maximal (7% on the 20th day after irradiation and bone marrow transplantation). After 10 days the histologic structure of the adenohypophysis was restored, and the dimensions of the secretory cells showed an increase, especially on the 40th day. After 90 days the histologic structure of the anterior pituitary of the lethally irradiated animals and of animals protected with bone marrow closely resembled the control picture.

Analysis of the nucleoplasmic ratio of the secretory cells of the anterior pituitary in the animals of group 3 revealed fluctuations of its value in all cells. In acidophils, for instance, the nucleoplasmic ratio was rather lower than in the control and was comparable with that on the 1st and 7th day, in basophils – on 1st, 2nd, and 40th days, and in chromophobes – on 2nd, 7th, 10th, and 40th days. The fluctuations observed both in the relative numbers of the different categories of cells of the anterior pituitary and in values of the nucleoplasmic ratio in lethally irradiated recipients at different times after bone marrow transplantation point to a functional strain on the pituitary.

This conclusion is confirmed by the results of determination of the serum corticosterone level in the lethally irradiated animals after bone marrow transplantation. As Fig. 3 shows, the serum corticosterone level in lethally irradiated recipients rose on the 3rd, 4th, 10th, and 40th days, and approached the control value on the 90th day. Changes in the blood corticosterone level of animals protected by bone marrow showed a wavelike fluctuation of the intensity of secretory function of the adrenal cortex, and they coincided in time with fluctuations of the number of chromophilic cells.

Under the influence of irradiation, the histologic structure of the anterior pituitary was thus disturbed in male mice; the character and severity of the disturbance depended on the time after irradiation, and dystrophic changes were observed both in the tissue of the gland itself and in the secretory cells. There was a change in the relative numbers of chromophils and chromophobes and their nucleoplasmic ratio. Other investigators also obtained similar results [3, 4].

Bone marrow transplantation reduced the intensity of the adverse effect of irradiation on the pituitary and helped to restore its normal histologic structure. Wavelike changes in the blood corticosterone level (corticosterone synthesis is under pituitary control) were observed in animals protected with bone marrow. Correlation was found between changes in the number of secretory cells in the anterior pituitary and the time course of changes in the corticosterone level in irradiated recipients protected with bone marrow.

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