ON TRANSPLANTATION OF "RADIATION" TUMORS OF THE MAMMARY GLANDS IN RATS

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There is evidence in the literature that tumors of the mammary glands [3], ovaries [2] and hypophysis [4, 5, 6], which arises as a result of radiation action from external sources, possess the ability to be transplanted, and thus, homotransplantation of radiation neoplasms can be used as a method for studying many individual questions in radiation oncogenesis. It appeared of interest to clarify to what degree this property is present in tumors caused by incorporated radioactive substances.

In this report, data are presented which were obtained from repeated, serial transplantations of mammary gland tumors, which had arisen in rats following their injection with radioactive niobium (niobium-95).

EXPERIMENTAL METHOD

The technique for reproducing tumors of the mammary glands by the use of radioactive niobium was described earlier [1]. Transplantation was carried out according to the widely accepted method: tumor tissue, taken from a living rat with observation of strict aseptic technique, was ground up in physiological saline until it formed a homogeneous suspension, and, using a syringe, 1 ml of the suspension was injected into the subcutaneous tissue of the back of the rat. For the first and all subsequent transplantations, 15 healthy female rats were used each time, weighing 60-80 grams. Subsequently, they were followed for the degree of viability and the rate of growth of the transplant. In addition, the developed tumors were studied morphologically, employing histological methods.

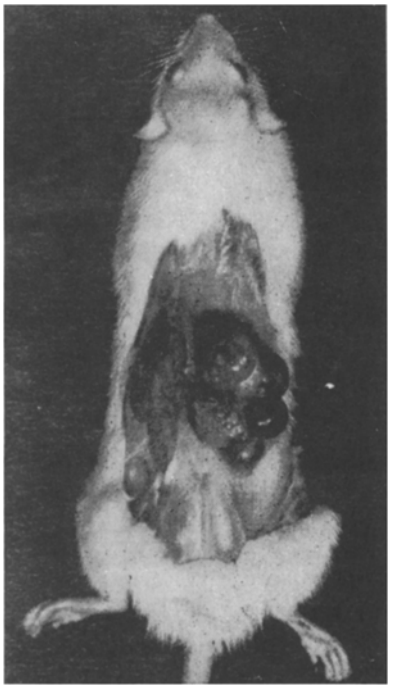

Fig. 1. External appearance of the 1st generation transplant.

EXPERIMENTAL RESULTS

Not all the mammary gland neoplasms possessed the same capacity for transplantation. Despite numerous attempts, injection of a suspension made out of benign tumors (fibroadenomas, adenofibromas) did not yield positive results. Adenocarcinomas of varying degrees of maturity transplanted well, as did certain of the adenomas with manifest tendency of the epithelium for proliferation. With injection of tumor tissue from one of the indicated structural variants, the transplant survived and began to grow in approximately half the cases (in 6 of the 15 rats). In the course of 35-45 days, it usually attained a large size (6-7 cm), representing a nodular tumor (Fig. 1), fixed to the skin and muscles of the back. The tumor was soft to the touch, and when cut into, showed a cavity filled with hemorrhagic or transparent fluid. On microscopic investigation, it was shown that the growing tumor differed in morphological structure from the original: it consisted, basically, of atypical epithelium, retaining its glandular structure in places, and a weakly expressed stroma, represented by fine collagen fibers. The rarely encountered vessels had thin walls and a dormant lumen.

Subsequent transplantations of a transplant of this structure were more successful. For example, the 4th generation transplant survived in all cases (in 15 of 15 rats), and the rate of growth increased by almost twice; within

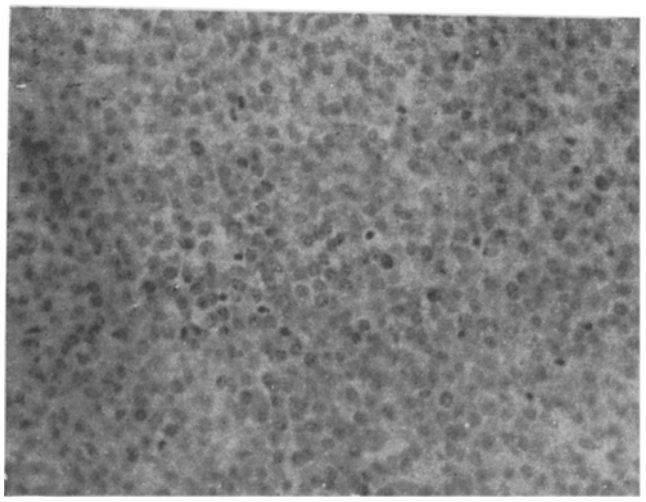

Fig. 2. Microscopic structure of the 4th generation transplant. Accumulation of monomorphic, atypical cells, with the absence of stromal elements. Stained with hematoxylin-eosin. Ocul. 10, obj. 20.

15-20 days, the tumor attained the same size as did the tumor of the 1st generation in 35-45 days. The external appearance of the transplant underwent major changes, now appearing as a gelatinous, pale nodule of elongated form and homogeneous consistency. On incision, we often observed hemorrhages and a cavity with hemorrhagic contents, pierced by filaments of fibrin. Often, the skin over the tumor was ulcerated, and the necrosis was not limited to the cutaneous covering, but extended deep into the tumor.

As a rule, growth of the tumor was accompanied by a progressing emaciation of the animals, especially in the far gone cases. Enlargement of the spleen, observed on autopsy in almost all the rats that were hosts for the transplants, is explained, to a certain degree, by the long-standing necrosis of the tumors. We often observed changes in the organs of the endocrine system: enlargement of the adrenals and, more often, of the thymus glands. Microscopic structure of the 4th generation transplant showed extremely anaplastic tissue, consisting of monomorphic, atypical cells with large, pale nuclei, and there was almost a complete absence of stromal elements (Fig. 2). The vessels, which were encountered rather rarely, had a sinusoidal type of structure and were congested with blood.

Finally, after the 5th generation, the transplant, still basically retaining the structure described, acquired a manifest capacity for metastasizing. On examining the animals, in all cases without exception we observed numerous metastases in the inguinal and axillary lymph nodes (Fig. 3), the subcutaneous tissue, the muscles of the peritoneal wall, the lungs, and the renal arches. According to histological structure, the metastatic tumor tissue was identical with its mother tissue, with the one difference that in the metastases, the cells showed hyperchromicity.

Thus, as a result of numerous transplantations of mammary gland adenocarcinoma, arising after injection of the animals with radioactive miobium, there occurred a gradual increase in the survival rate of the transplant, and an acceleration in its growth. Morphologically, this phenomenon was expressed in a progressive anaplasia of the tumor tissue, which turned into undifferentiated, immature tissue. The transplant of such structure possessed a high metastatic activity, which was never observed in the previous generations, let alone the tumors of the "originals", i.e., those which were directly induced by the isotope.

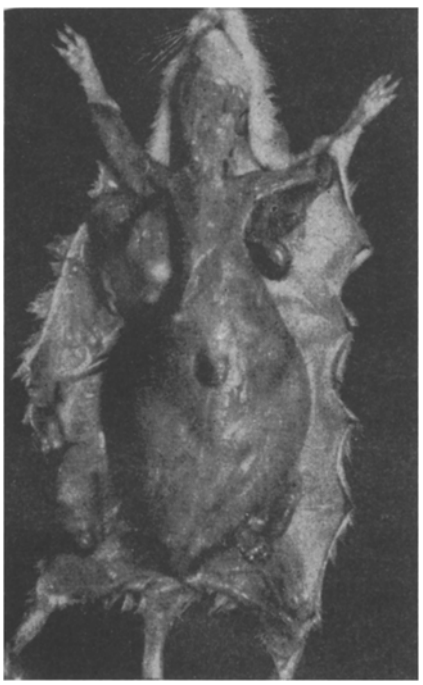

Fig. 3. Metastases in the inguinal and axillary lymph nodes.

An increase in the degree of malignancy of tumors following multiple transplantations is a fact that is already known. G. F. Gamperl' [7] calls this phenomenon the "progression" of the tumor, implying in this term the loss of the tissue's capacity to differentiate, the rapid transition to the stage of infiltration and metastasis, and also transition from dependency to independency, i.e., to greater autonomy. We cannot confirm that the "radiation" tumors of the mammary glands acquire independence in the process of transplantation, since in this case we did not have objective tests, such as exist, for example, with transplantation of tumors of the hypophysis [4], which produce ACTH (obesity, polyuria, glucosuria, lymphocytopenia, hypertrophy of the adrenal cortices, etc.). Nevertheless, the vigorous growth, progressive anaplasia, and high metastatic activity of the transplant, which we observed in our experiments, testified to its marked autonomy. In addition, by means of subsequent transplantations, apparently, it would be possible to produce a transplant strain of tumor cells like those which are used in experimental oncology at the present time.

The results of this investigation bear evidence that mammary gland

tumors, arising from the entrance of radioactive isotopes into the organism, do not differ in their biological properties from neoplasms of the mammary glands which are caused by other cancerogens (of non-radiation nature). In other words, the "radiation" tumors of the mammary glands in rats are not characterized by any kind of specificity.

SUMMARY

Adenocarcinoma of the mammary glands, occurring after the administration of radioniobium to rats are transplantable to other rats. With further transplantations there occurs a gradual rise in the rate of the transplant growth and of its "take". In morphological respect this phenomenon is characterized by progressive anaplasia of the tumor tissue. After the 5th generation the transplant became capable of metastasization to many internal organs. A rise in the area of the mammary gland transplant in repeated successive transplantations lies at the basis of this phenomenon.

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