DEVELOPMENT OF MAMMARY TUMORS IN RATS AFTER PARENTERAL ADMINISTRATION OF NIOBIUM-95

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The successes obtained in studies of the biological effect of ionizing radiation provided the experimental oncologists with one more method to reproduce malignant growth experimentally. Neoplasmas of almost all organs and systems have been obtained and described in experiments on animals exposed to radiation.

In recent years, research workers pay increasing attention to the carcinogenic effect of incorporated radioactive elements. It is well known that certain isotopes are capable of accumulating selectively in one or the other organ (the so-called bone group and liver group of isotopes) and their prolonged presence in the tissues leads to the development of malignant growth in the particular organ which is exposed to the in action. In addition, a group of "evenly" distributing radioactive substances has been described (Niobium-95, Cesium -137, and Rhutenium-106) which cause tumors in the endocrine glands and other tissues. Among the latter, tumors of the mammary glands are of particular interest. In the literature devoted to this question, tumors have been described which develop after exposure to x-rays, γ-rays, [5-7, 10, 16, 17], neutrons [10], and after local application of substances emitting β-radiation [15], after introduction of Ag-110 [2], and thorium [5] into the glandular tissue, and after incorporation of astatin-211 [8].

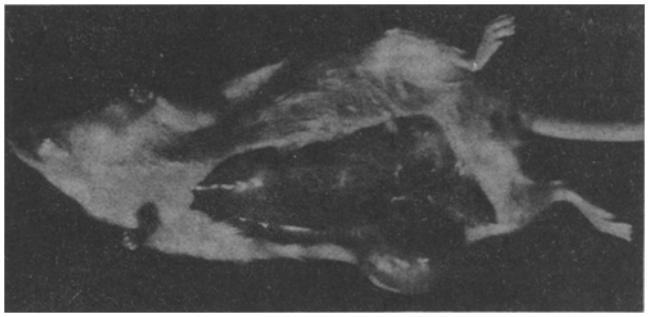

Fig. 1. The external appearance of a mammary tumor developing in a rat 164 days after intraperitoneal injection of Niobium-95.

V. N. Stel'tsov and Yu. I. Moskalev [4] were the first to describe cases of mammary tumors developing after the administration of a radioactive element: Niobium-95.

Niobium-95, as is well known, emits relatively soft β-radiation and γ-radiation (E max 0.14 and 0.75 Mev.); the element has a half-lifetime of 35 days. After intraperitoneal injection it is quickly resorbed and evenly distributed in the body, forming complexes with the plasma- and tissue proteins. Niobium is present for a relatively short time in the body: half of the substance is excreted within about three weeks and in consequence the intensity of tissue exposure to radiation is highest during the first 32 days and then quickly decreases. Within 150 days Niobium is practically eliminated from the body [1].

As we were in the possession of certain data in this field, we set ourselves the task to attract in the present investigation the attention of the research workers to this reliable and, in our opinion, easily reproduceable model of malignant growth.

EXPERIMENTAL METHODS

210 female white rats weighing 130-160 g were used for the experiments. Niobium-95 oxalate with an activity of 6 mC/g was administered by intraperitoneal injection. Twice in a month the experimental animals were thoroughly investigated. If tumors were detected the rats were immediately killed and the tumorous nodes were studied by the usual histological methods.

EXPERIMENTAL RESULTS

The animals were observed for 700 days and in the course of this period tumors were found in 73 rats, which constitutes 38.8%. During the latency period, which was equal to 164 days, 22 rats (11%) perished under symptoms of subacute and chronic radiation sickness. The occurrence of spontaneous mammary tumors in rats varies between 12 [4] and 20.6% [3]; these tumors usually develop in old rats (after 400 days) and are, as a rule, not of multiple character.

In our experiment, the mammary tumors represented nodes of spheroid shape, surrounded by a capsule and situated in the subcutaneous tissue near the nipple (Fig. 1). The consistency of the neoplasma and the external appearance on cross sections varied from a grossly lobular cartilage-like structure to a pasty homogenous mass, frequently interspersed with hemorrhages. Sometimes a dense liquid, resembling the color of milk, was flowing from the section surface and in these cases the tumor tissue had a coarse alveolar structure.

In 61 rats the tumors were of solitary, and in 12 rats of multiple character: two nodes developed in 6 rats, three nodes in three rats, four nodes in one rat and five nodes in two rats. Multiple tumors appeared not before 350 days had elapsed and their morphological structure was not always identical. It is so far difficult to state whether these tumors all developed simultaneously or in a certain order.

Our material thus included a total of 96 tumorous nodes. Among these, the greatest group consisted of adenomas (56.5%) showing a varying relation between stroma and parenchyma: fibroadenomas, adeno-fibromas, and simple adenomas containing relatively little stroma and showing a marked tendency to epithelial proliferation (Fig. 2).

Morphologically this latter form was closely related to the adenocarcinomas (23.9%) which showed marked signs of immaturity and infiltrative growth (Fig. 3). Fibrocystic mastopathia was found in 17.4% of cases and polymorphocellular sarcoma in 2.2% of cases.

We never observed metastasis formation in other organs. This was possibly due to the fact that the animals were killed immediately after the tumors had been detected. The regional lymph nodes were frequently enlarged and showed a greater or lesser degree of hyperplasia.

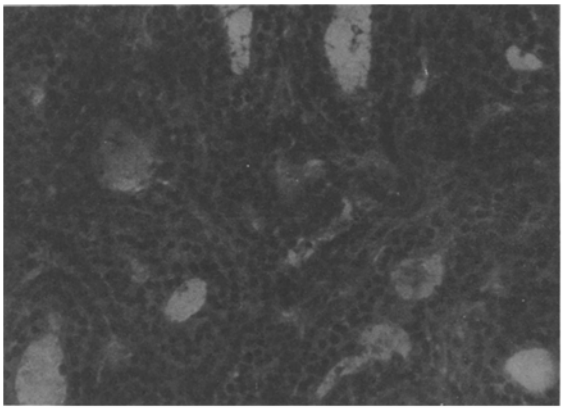

Fig. 2. Simple mammary adenoma developing 174 days after injection of Niobium-95. Hematoxylin-eosin stain. Magnification: eye piece ×10, objective ×20.

Fig. 3. Adenocarcinoma showing infiltrative growth of the atypical epithelium developing 522 days after the injection of Niobium-95. Hematoxylin eosin stain. Magnification: eye piece ×10, objective ×10.

When transplanted into other rats, the adenomas and adenocarcinomas showed a marked ability to grow. It seems that the "Niobium tumors" of the mammary glands are a suitable object of investigation from this point of view as well.

The dyshormonal origin of mammary tumors is at present well known. It seems that from this point of view the "radiation" tumors do not represent an exception [17].

In our experiments, mammary tumors were frequently accompanied by various changes of the endocrine organs. Autopsy of animals at various stages of tumor development revealed a considerable increase in the size of the uterine horns and the horns were filled with serous liquid due to the impaired outflow caused by hyperplasia of the

uterine mucosa. After 350 days the mammary tumors were fairly frequently accompanied by various neoplasmas in the ovaries and, beginning from 450 days, chromophobic pituitary adenomas were a frequent finding at autopsy. The experimental use of Niobium-95 thus offers far-reaching possibilities not only for studies of the malignization of the glandular tissue and the pattern of malignant growth but also with regard to the production of endocrine disorders which finally lead to the development of tumors.

SUMMARY

Eleven per cent of female albino rats died within 164 days with phenomena of subacute and chronic radiation sickness as a result of niobium-95 administration (MC/gm). Solitary and multiple mammary gland neoformations of different morphological structure have occurred in 38.8 per cent of the survived animals (mastopathies, adenomas, adenocarcinomas, sarcomas). Adenomas, and especially adenocarcinomas were transplantable. Beginning from the 350th day the mammary gland tumors were not infrequently associated with ovarian tumors, and after the 450th day – with tumors of hypophysis. This points to the dyshormonal origin of the radiation mammary gland tumors.

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