

THE DEVELOPMENT OF TUMORS OF THE MAMMARY GLANDS IN RATS

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There are indications in the literature of the frequent (up to 36%) appearance of fibroadenomas of the mammary glands in old virgin rats [1].

While studying destructive changes in the liver produced in rats by chronic poisoning with carbon tetrachloride, we observed in many experimental animals the development of tumors of the mammary gland. These tumors were subjected to histological examination. The results of this investigation form the subject of the present communication.

EXPERIMENTAL METHOD

The experiments were carried out on virgin female white rats, one year old, with an initial body weight of 230–270 g. Sixty-five animals were used in the experiment, of which 40 were experimental and 25 control. The experimental rats were injected subcutaneously twice a week with 0.2 ml of CCl_4 for a period of $9\frac{1}{2}$ months.

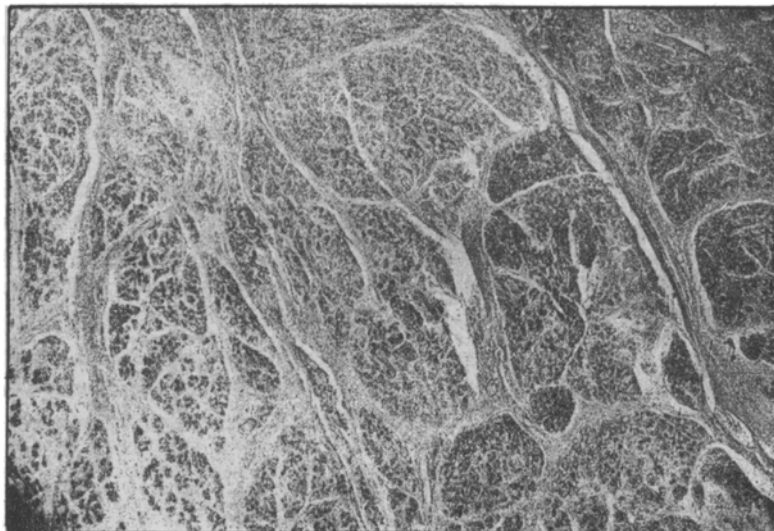


Fig. 1. A young tumor developing in a rat after 5 months 18 days of injections of CCl_4 . Stained with hematoxylin-eosin. Magnification: ocular 6 X, objective 8.



Fig. 2. Fibroadenoma. Proliferation of connective tissue. Presence of alkaline phosphatase (Gomori's method). Magnification: ocular 8 X, objective 20.



Fig. 3. Fibroadenoma. Presence of alkaline phosphatase (by Gomori's method). Magnification: ocular 8 X, objective 12.

After this period of time had elapsed the injections of CCl_4 were discontinued and the rats were kept in their cages on an ordinary balanced diet. Throughout the whole period of the experiment the control rats received no injections. The experiment lasted 375 days. Experimental rats were killed at different times which were determined by the development of the tumor. The tumor was freed from surrounding tissues and weighed. Pieces of tumor were fixed in 80° alcohol and in Carnoy's fluid. The material was embedded in paraffin wax by the usual method. Sections, 8-10 μ in thickness, were stained with hematoxylin-eosin and by Mallory's method. The alkaline phosphatase was estimated by the Gomori (1939) method; ribonucleic acid (RNA) was detected by staining the sections with methyl green-pyronin by Unna's method.

EXPERIMENTAL RESULTS

During our observations on the experimental animals we observed the development of a tumor of the mammary gland in 24 of the rats (60%) which were given injections of CCl_4 . The tumor was usually localized to the region of the superior or posterior limbs (2nd or 5th pairs of nipples).

The first tumor appeared in rat No. 15 after 5 months 18 days of injections of CCl_4 . The animal was killed; it weighed 230 g. The tumor, developing in the region of the right forelimb (2nd pair of nipples), was the size of a large walnut; it was easily separated from the surrounding tissues, and weighed 23 g. The tumor was firm, pinkish white in color, and cut with difficulty with scissors. On section white nodules could be seen, of different sizes and resembling cartilage.

Histological study of sections of the "young" tumor showed that the glandular tissue was preserved to a considerable extent, but many lobules had undergone degenerative changes. The lobules were connected by broad bands of coarse, fibrous connective tissue (Fig. 1). In isolated areas of the gland there appeared a large amount of coarse, hyalinized connective tissue, among which was preserved a very insignificant amount of glandular epithelium.

In the remaining 23 animals tumors developed in the 10th-12th month after the beginning of the experiment. The tumors grew slowly and were readily separated from surrounding tissues. The rats were killed at different periods of growth of the tumor. The weight of the tumors varied from 21 to 134 g. The "young" tumors were the size of pigeons' eggs and consisted of dense, white tissue, which cut with difficulty with the scissors; foci of necrosis were not present in these tumors. The "old" tumors reached the size of an apple, contained areas of hemorrhage, were soft to the touch, and on section they yielded milk, mixed with blood and pus. The lactiferous ducts were dilated (Fig. 2). Foci of necrosis in the tumor were mingled with areas of dense connective tissue. The blood vessels were markedly hyperemic. Inflammatory foci were encountered; in these cases the appearance of a large number of lipoid cells was observed.

Determination of the content of alkaline phosphatase and RNA showed that the nuclei of the epithelial cells of the alveoli were characterized by considerable enzymic activity; the nucleoli were rich in RNA, and the cytoplasm contained a small quantity of enzyme and RNA. The cytoplasm of some epithelial cells of the alveoli were intensely vacuolized; no enzyme nor RNA was observed in the vacuoles. The secretion in the lumen of the terminal sections was rich in alkaline phosphatase and RNA. In the connective tissue only the nuclei gave a positive reaction for alkaline phosphatase (Fig. 3).

In the control rats the development of a tumor of the mammary gland was observed in only one case (4%).

Macro- and microscopic examination showed that the tumor developing in the mammary gland of the experimental and control rats is a fibroadenoma. We believe that the prolonged action of injections of CCl_4 creates favorable conditions for the formation of a fibroadenoma of the mammary gland in rats.

SUMMARY

Fibroadenoma of the mammary glands appeared in 24 of the 60 rats which received subcutaneous injections of carbon tetrachloride for $9\frac{1}{2}$ months. It is assumed that prolonged administration of this chemical creates favorable conditions for development of tumors of the mammary gland.

LITERATURE CITED

- [1] E. L. Prigozhina, *Arkh. Patol.*, 1, 109-110 (1956).