THE EFFECT OF ASEPTIC PROLIFERATIVE INFLAMMATION ON THE LOCALIZATION AND GROWTH OF SPONTANEOUS TUMORS OF THE MAMMARY GLANDS IN MICE OF THE HIGH-CANCER C_3HA STRAIN

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There is insufficient reliable information at the present time to be able to assert that inflammation or an inflammatory reaction retards the growth of tumors. With a view to further study of the effect of inflammation on the growth of tumors we carried out experiments on mice of the C_3HA strain, which we obtained from R. E. Kavetskii's laboratory in Kiev. Tumors in mice of this strain are caused by a virus-like agent, which is transmitted along the maternal line through the milk of the lactating females; this agent has been called "milk factor". According to the observations of N. M. Turkevich [13], almost all female mice of this strain develop spontaneous cancer of the mammary gland at the age of 7-8 months.

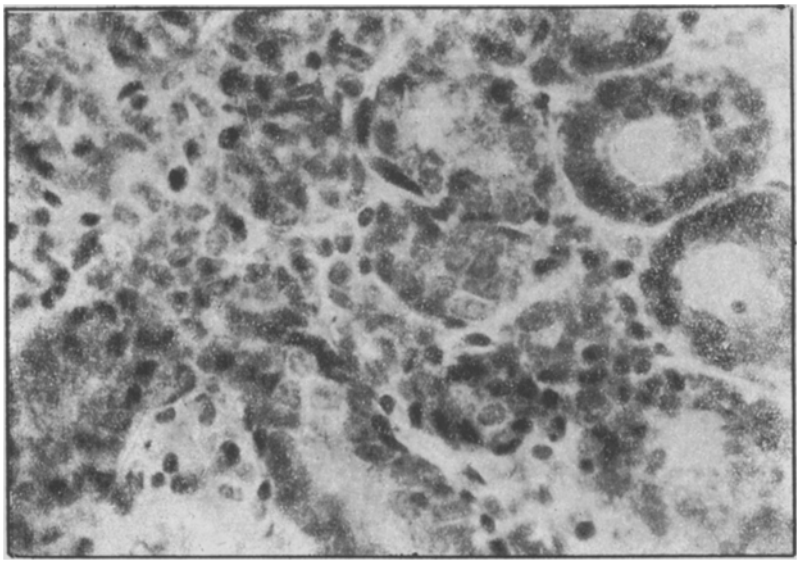

Fig. 1. Proliferation of the glandular epithelium of the mammary gland of a female mouse. Magnification 500.

In spite of adequate study of the etiology and the histological structure of spontaneous tumors in this strain of mice [4, 5, 13, 14, 15, 16], extremely little attention has been given to ascertaining the effect of inflammation on the growth and the course of spontaneous tumors of the mammary glands. The investigation of the influence of inflammation on the localization and growth of the spontaneous carcinoma of the mammary gland of virus

origin is of particular importance nowadays, when the virus etiology of tumors is receiving ever-increasing attention in both the Soviet and foreign literature [2, 3, 10, 11, 12, 16 and others].

EXPERIMENTAL METHOD

For the production of a proliferative inflammatory lesion, an injection of 0.3 ml of a 10% solution of an emulsion of infusorial earth in peach oil was given through a fine needle into the region of the left mammary gland of the fifth posterior pair in female mice at the age of 3 months. From 2-3 days later some swelling and erythema of the skin were observed at the site of injection.

One month after the injection of the 10% solution of emulsion of infusorial earth, at histological examination of the mammary gland a sluggish proliferative inflammatory lesion was observed around the acini and ducts of the mammary gland. Proliferation of young connective tissue cells (histiocytes, fibroblasts, polyblasts) and endothelioid cells, and accumulations of reticular cells and segmented polymorphonuclear leucocytes were seen. A well-marked proliferation of the glandular epithelium of the mammary gland was observed. The glandular epithelium was swollen and its apical part palely stained, and containing fine granular inclusions. In the lumen of the glands were masses of small granules, stained a pink color, and desquamated cells of the glandular epithelium. Histological diagnosis – a proliferative inflammatory lesion of the mammary gland (Fig. 1).

At the age of 5 months the same female mice were injected once again in the same region (corresponding to the fifth posterior pair of mammary glands, on the left side) with 0.3 ml of the 10% solution of the emulsion of infusorial earth in peach oil. The experiment was performed on 80 female mice. Eighty female mice of the same strain, which were not injected with the 10% solution of the infusorial earth emulsion into the mammary gland, acted as controls. It should be mentioned that the experimental and control mice were kept in identical conditions.

EXPERIMENTAL RESULTS

As seen from the figures in the Table, in the experimental group consisting of 80 mice spontaneous tumors of the mammary glands were seen in 61 mice, and in the control group adenocarcinoma of the mammary glands was found in 53 mice. In the remaining mice no spontaneous neoplasms were found after observation for two years. In the experimental group of mice multiple spontaneous neoplasms of the mammary glands were most commonly seen, in contrast to the analogous group of control mice. Multiple tumors were seen in 18 cases in the experimental group of mice, and only in 7 cases in the control group.

Still clearer was the difference between the experimental and control groups of mice in respect to the incidence of lung metastases from an adenocarcinoma of the mammary gland. Multiple metastases from carcinoma were observed in the lungs of mice of the experimental group in 17 cases, and in the control group of mice in only 8 cases. The sluggish inflammatory proliferative lesion also had a perceptible influence on the time of appearance of the spontaneous tumors of the mammary gland. The times of appearance of the first tumors in the mammary gland of the experimental and control groups are shown in Figure 2.

From the results given it follows that the greatest number of mice affected by tumors in the experimental group was at the age of 8-10 months. At the age of 8 months, for instance, spontaneous adenocarcinomas of the mammary gland developed in 12 mice, and at the age of 9 months – in 21 mice. In the following months of life of the mice the tumors developed more rarely. It must be pointed out that the first tumors in the experimental

The Influence of Proliferative Inflammation on the Growth of Spontaneous Tumors of the Mammary Glands

Group of mice	Total no. of mice	Number of mice			
		with spontaneous tumors	with multiple cancerous lessions	with metastases in the lungs	no tumor found
Experimental	80	61	18	17	19
Control	80	53	7	8	27

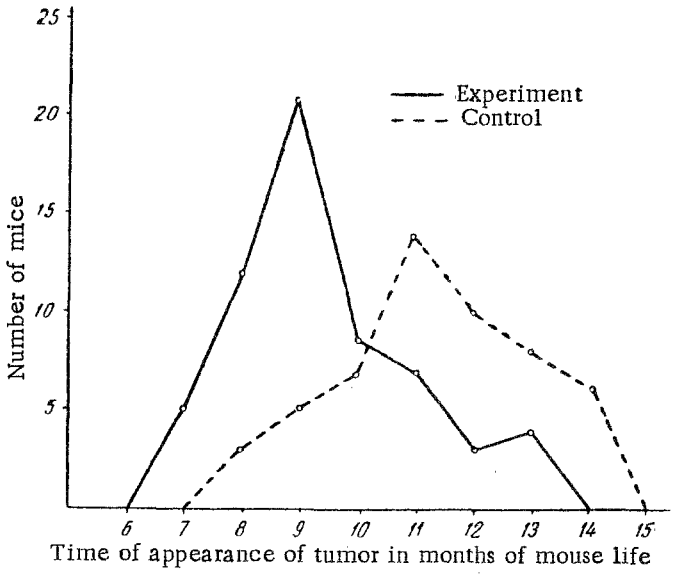

Fig. 2. Curve showing the appearance of spontaneous tumors of the mammary gland in mice of the high-cancer C_3HA strain, in relation to age.

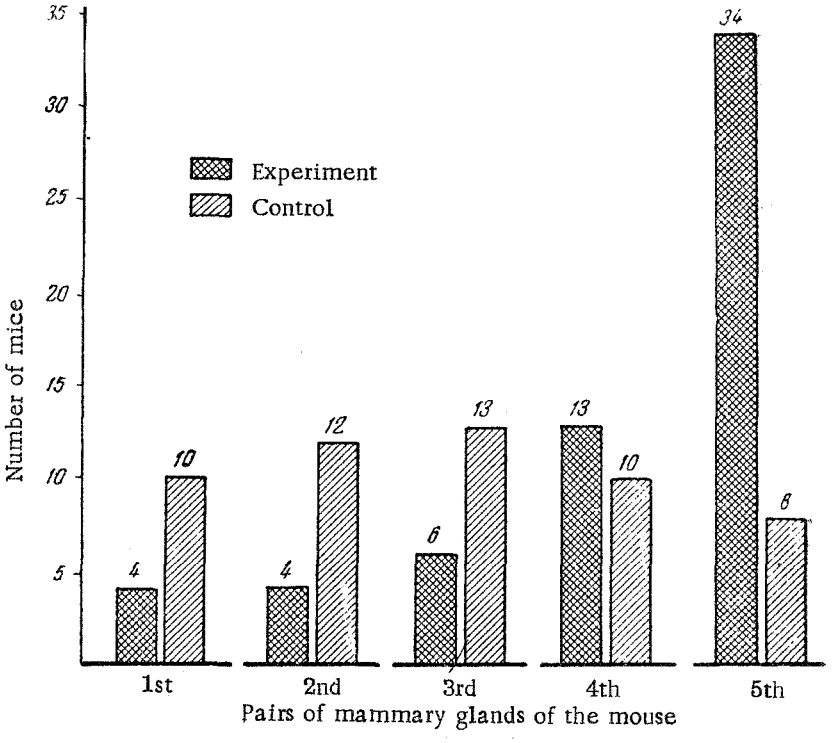

Fig. 3. Localization of spontaneous tumors of the mammary glands in mice.

Note: Where multiple carcinoma was present in 4 mice, only the location of the first tumor to appear is shown on the Figure.

group of mice were apparent at the age of 7 months, but in the control group of mice the first tumors were apparent only at the age of 8 months.

In the control group the greatest number of mice was affected with tumors at the age of 11-12 months.

At the age of 11 months tumors appeared in 14 mice, and at the age of 12 months – in 10 animals. From the results obtained it follows that a sluggish inflammatory process causes a number of changes in the body, bringing about earlier development of spontaneous tumors than occurs in the group of control mice.

The sluggish inflammatory lesion also had a perceptible effect on the localization of the spontaneous tumors of the mammary glands (Fig. 3).

The findings shown in Figure 3 show that spontaneous tumors developed most commonly in the region of the fifth pair of mammary glands, where the sluggish proliferative inflammatory lesion had been produced. In the experimental group of animals tumors appeared in the posterior pair of mammary glands (4th and 5th pairs) in 47 of 61 mice; in the anterior pairs of mammary glands spontaneous adenocarcinomas were found in only 14 cases. In 53 control mice with spontaneous tumors, adenocarcinomas were discovered in the posterior pairs of mammary glands (4th and 5th pairs) of 18 mice, and in the anterior pairs (1st, 2nd and 3rd pairs) of 35 mice. It must be pointed out that of the 34 mice in which spontaneous neoplasms arose in the region of the 5th pair of mammary glands, in 28 cases the tumors were found in the region of the left gland, where the proliferative inflammatory lesion had been produced.

The experiments carried out on 160 mice of the C_3HA strain give us the right to state that a proliferative inflammatory lesion has a perceptible influence on the localization and time of appearance of spontaneous tumors of the mammary glands. The neoplasms in the mice with an inflammatory focus appeared at an earlier age and were more often multiple in form than was the case in the control group of animals. The experimental results obtained showed that for the pathogenicity of the virus causing spontaneous tumors of the mammary glands in mice of the C_3HA strain to become apparent, suitable conditions are necessary. One of the more important of the conditions for the development of tumor viruses is probably the formation in the body of foci of cellular proliferation, which in our experiments were caused by sluggish proliferative inflammatory lesions.

SUMMARY

Experiments were performed on 160 female mice of the highly cancerous strain C_3HA with the so-called "milk factor". These experiments were aimed at studying the effect of proliferative inflammation on the growth of cancer. This proliferative inflammatory process was induced by the injection of 0.3 ml of 10% emulsion of infusorial earth in peach oil. At the age of 5 months the same mice received a repeated injection of 0.3 ml of 10% emulsion of infusorial earth in peach oil into the same site. Experiments demonstrated that the inflammatory process considerably affected the localization and the time of appearance of the tumors of the mammary glands. The neoplasms most frequently occur in the mammary gland affected by the proliferative inflammatory process. These neoplasms appeared in younger mice in comparison with the analogous group of control animals. The author assumes that the foci of the cellular proliferation caused by the inflammatory process create favorable conditions for manifestation of pathogenicity of the virus causing spontaneous cancer of the mammary gland.

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