TUMORS INDUCED BY METHYLCHOLANTHRENE IN THE STEPPE LEMMING. A TRANSMISSIBLE STRAIN OF LEMMING SARCOMA (LS)

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Recently the steppe lemming (Lagurus lagurus Pall.), a small rodent used for several years in work on tularemia and listeriosis [2], has recently been used as an object for experimental oncological research [1, 3, 4]. Because of its ease and rapidity of multiplication and the simplicity of its care and feeding, as well as its resistance to mouse ectromelia, it has been found to be a convenient laboratory animal. The results of our first experiments [5], in which we used a carcinogenic compound [9:10-dimethyl-1:2-benzanthracene (DMBA)] and heterotransplantation of tumors, show that the steppe lemming is suitable for experimental oncological research.

The aim of this work was to test the sensitivity of the steppe lemming to the action of another carcinogenic compound – methylcholanthrene (MC)—whose carcinogenic properties are less pronounced than those of DMBA. We also aimed to inoculate tumors induced by MC in order to obtain a transmissible strain of the tumor.

METHOD

Experiments were carried out on 32 animals (15 females and 17 males) aged from one to 16 months, which received subcutaneous injections of a 0.5% solution of MC in peach oil in a dose of 0.2 ml. Each animal received 1 mg of the compound. The tumors which developed were inoculated into young lemmings at about one month of age. For inoculation, a suspension of tumor tissue in physiological saline was injected subcutaneously and, in subsequent generations, intramuscularly also

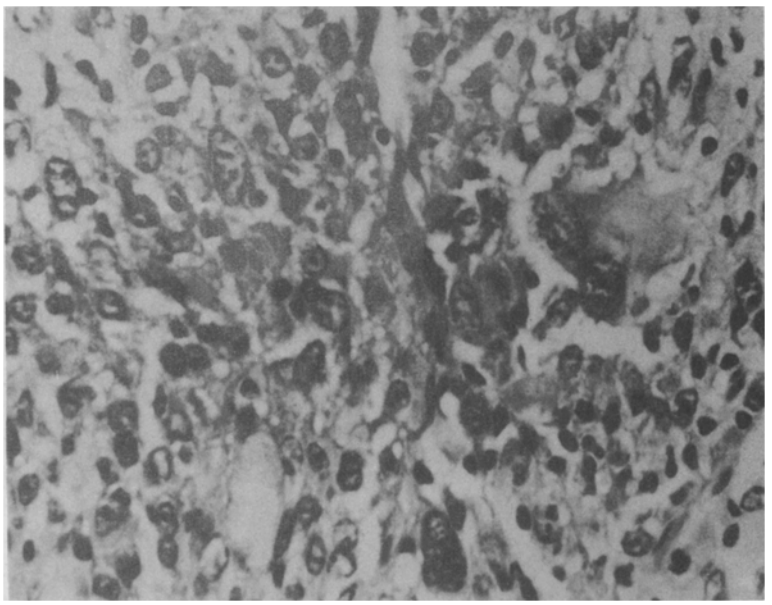

Fig. 1. Polymorphocellular sarcoma in a lemming. Stained with hematoxylin-eosin. Magnification 500×.

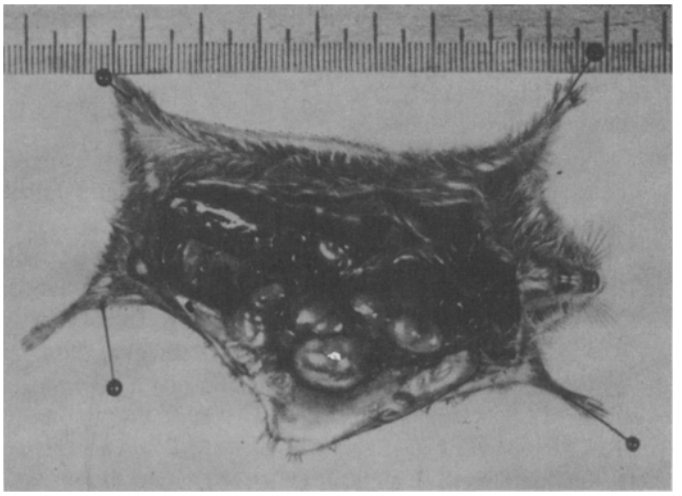

Fig. 2. Tumor, inoculated subcutaneously (first 5 generations).

in a dose of approximately 0.4-0.5 ml. For histological investigation, all the tumors were fixed in 10% formalin and sections were stained with hematoxylin-eosin and by Van Gieson's method.

RESULTS

The first tumors were observed four months after the beginning of the experiment, and they continued to appear throughout the next 11 months. Of the 32 animals taking part in the experiment, 24 survived until the time of appearance of the first tumor. Tumors developed in 13 of these animals (54%). In two animals, tumors developed between four and five months from the start of the experiment, in one after five to six months, in three after six to seven months, in one after seven to eight months, in five after eight to nine months, and finally, in the last after 11 to 12 months. The largest number of tumors (9 of 13) developed between six and nine months. Tumors developed in the animals independently of their sex and initial age. The longest period of survival of lemmings with tumors was two months. This period, however, is possibly not the upper limit, for we sacrificed most of the lemmings with tumors in order to inoculate these.

Histological investigation of the tumors which developed showed that 12 of the 13 were polymorphocellular sarcomas and one was an adenosarcoma. In all the polymorphocellular sarcomas many giant cells and mitoses were seen. No metastases were found in the lymphatic glands, the lungs, or other organs.

On comparison of our findings with those of E. E. Pogosyants [4], who gave lemmings a subcutaneous injection of 0.5 mg of DMBA, it is apparent that the incidence of development of tumors in the first (54%) and second (52.5%) cases was roughly the same. The difference between the action of DMBA and MC was shown only by the fact that, after DMBA, the tumors developed in a shorter period of time. After injection of DMBA the first tumors appeared three months from the start of the experiment, and the largest number of tumors (8 of 12) appeared 4-5 months from the start of the experiment.

Nine of the 13 tumors developing in our experiment were inoculated in other animals. Two of the nine tumors were unsuccessfully inoculated in the first generation. One of these initiated a strain which is described below, while the other was not transplanted further.

Strain LS (lemming sarcoma). The original tumor developed four months from the start of the experiment in an eight-month-old female. The tumor was the size of a large hazelnut, not very firm, with some degree of destruction in the center. In its morphological structure the tumor was a polymorphocellular sarcoma (Fig. 1).

In the first five generations, the tumor was inoculated subcutaneously (Fig. 2). The percentage of successful takes was small (47). After the sixth generation the tumor was inoculated intramuscularly, into the left hind limb. The proportion of successful inoculations by this method was higher, and in order to secure more rapid adaptation, we changed over to intramuscular inoculation.

The percentage of successful inoculations of the tumor by the intramuscular method, investigated for 26 generations, was 82.3. The spontaneous absorption rate was 7%. Only nodules and small tumors were absorbed. No absorption of middle-sized and large tumors was observed. In no case were metastases found.

The earliest time at which death of an animal with a tumor was observed was the 11th day, and the latest the 26th day after inoculation. The average duration of survival of lemmings with tumors was 14-16 days. The tumor was inoculated on the 8th-9th day.

In the 17th generation the tumor was again inoculated subcutaneously, and subsequently the two substrains were inoculated simultaneously—subcutaneously and intramuscularly. After intramuscular inoculation, the rate

of successful subcutaneous inoculation of the tumor, investigated for the first ten generations, was 90%, but the absorption rate of the tumors was much higher (19%) than after intramuscular inoculation. The mean duration of survival of the lemmings with tumors after subcutaneous inoculation was slightly longer (16-20 days).

No significant changes took place in the morphological structure of the tumor in the process of the inoculations.

SUMMARY

It is shown that tumor development in the steppe lemming (Lagurus lagurus Pall.) can be induced by subcutaneous administration of methylcholanthrene (1 mg).

A strain of transplantable polymorphocellular sarcoma of these animals is described.

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