

SPONTANEOUS MAMMARY GLAND TUMORS OF DOGS
AS A MODEL FOR EXPERIMENTAL TUMOR THERAPYN. E. Osipov, N. D. Lagova,
and V. I. Ponomar'kov

UDC 618.19-006-021.3-092.9-08.001.57

The effectiveness of various hormonal procedures (ovariectomy, prolonged administration of androgens) on growth of spontaneous mammary gland tumors in dogs was studied. Mammary gland tumors in dogs were found to be markedly dependent on hormones and a change in the hormonal balance of the body by the above methods led to a three- to fourfold increase in the period of survival and to a decrease in the mortality of the animals from the underlying disease. The results suggest that this type of neoplastic disease in dogs can be used as a model for research in the field of experimental tumor therapy.

Nearly one-half of all spontaneous tumors in dogs arise in the mammary glands. Their development, as the writers' earlier investigations have shown, is largely determined by hormonal factors [1]. The question of the experimental treatment of mammary gland tumors in dogs has received very little investigation. The only work known to the writers is that of Huggins and Moulder [3], who attempted unsuccessfully to use hormone therapy, in the form of ovariectomy and adrenalectomy, to treat neoplasms of the mammary glands.

The object of the investigation described below was to obtain experimental evidence relating to the use of spontaneous mammary gland tumors in dogs as a model for the research into tumor therapy. Methods known to be effective against carcinoma of the human breast were used on the grounds that only by the investigation of similar procedures under clinical and experimental conditions can the adequacy of the reactive properties of mammary gland tumors in dogs and man be judged to the fullest extent.

EXPERIMENTAL METHOD

From 168 dogs with mammary gland tumors 59 of about the same age (8-9 years) and with a similar clinical picture (a large tumor nodule and one or two small nodules close to it without metastases in the internal organs), and with histological confirmation of the diagnosis of mammary gland carcinoma, were chosen. Methods of hormone therapy such as ovariectomy, in order to suppress the estrogenic functions of the ovaries, and ovariectomy combined with prolonged administration of androgens were used.

Mastectomy alone was carried out on a group of animals consisting of 23 dogs (group 1 - control); mastectomy was combined with simultaneous ovariectomy on 18 dogs (group 2), while another 18 animals, after mastectomy and ovariectomy, received repeated injections of testosterone propionate, in the form of compressed pellets weighing 1-3 g, by implantation into the subcutaneous areolar tissue or under the aponeurosis on the lateral surface of the trunk, at intervals of 3-4 months (group 3). The doses of testosterone were calculated relative to the dog's body weight and were equivalent to the doses used clinically [2]. The effectiveness of the measures was judged from the length of survival of the animals after the

Animal Cancer Clinic and Laboratory of Experimental Endocrinology, Institute of Experimental and Clinical Oncology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Blokhin.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 74, No. 8, pp. 81-82, August, 1972. Original article submitted July 5, 1971.

© 1973 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

operation and the onset of recurrences or the appearance of new tumor nodules in other glands. In addition, observations were made on the state of the small tumor nodules, especially left behind in some cases during mastectomy and subsequently used as an indicator of the effectiveness of treatment.

EXPERIMENTAL RESULTS

The general state of the dogs of group 1 remained good during the first 3-5 months after the operation, but later they developed tumors in other mammary glands or, less frequently, recurrences in the scar. All animals except two died from progression of the underlying disease with evidence of generalization and metastasization in the internal organs, as confirmed by autopsy. The mean life span of the animals of this group was 6.1 months. Of the 18 dogs in group 2, nine died from progression of the underlying disease with metastasization in the internal organs 8-9 months after the operation; three dogs died from unknown causes outside the clinic; four dogs were still alive 12-18 months after the operation (September 1, 1970) and their condition remained good. The mean life span of the animals of this group was 18.5 months. Of the 18 dogs in group 3 five died after 3-3.5 years from metastasization in the internal organs, six from unknown causes, and seven were alive, four of them in a good condition, more than 3 years after the operation. The mean life span of the animals of this group was 29.4 months.

These results show that the survival of the ovariectomized dogs was almost three times longer than that of dogs undergoing mastectomy alone. Prolonged administration of testosterone propionate lengthened the survival of the animals by more than four times compared with the control. In group 1 nearly all the animals died from progression of the underlying disease, while, in groups 2 and 3, nine and five animals, respectively, died from the underlying disease, but much later. Ovariectomy evidently delays growth of the tumors in dogs, especially if testosterone is administered. In addition, the control nodules remained unchanged in the dogs of group 3 throughout the period of observation.

It can be concluded from this investigation that spontaneous mammary gland tumors in dogs can be used as a model for the testing of new hormonal preparations and methods of medical treatment. However, such tests should be carried out on animals with localized forms of the disease, when the tumor is still hormone-dependent. Failure to observe this condition may well be the reason for the unsuccessful attempts at hormone therapy of spontaneous mammary gland tumors in dogs.

LITERATURE CITED

1. V. I. Ponomare'kov and N. E. Osipov, in: *Current Problems in Oncology* [in Russian], No. 2, Moscow (1970), p. 34.
2. O. V. Svyatukhina, in: *A Handbook of Oncology* [in Russian], Moscow (1964), p. 261.
3. C. Huggins and P. Moulder, *J. Exp. Med.*, 80, 441 (1944).