

# EFFECT OF TOTAL AND SUBTOTAL THYROIDECTOMY ON GROWTH OF TRANSPLANTED GLIOBLASTOMA MULTIFORME OF THE RAT CEREBELLUM

N. A. Spryshkova

UDC 616.831-006.484-092.9-092:616.441-089.87

Subtotal and total thyroidectomy lengthen the incubation period of the disease in rats inoculated with a glioblastoma multiforme of the cerebellum and delay the animals' death by several days.

In the study of the mechanism of carcinogenesis and development of effective methods of combined treatment of malignant tumors there is a strong case for assigning a leading role to the endocrine glands and hormone therapy. Rational hormone therapy is based primarily on results indicating to what extent the endocrine system participates in the pathogenesis of a malignant disease or in the development of reactions against the tumor.

According to Avtsyn's concepts [1], hormonal agents play an essential role in the development of tumors of the central nervous system. There is reason to suppose that the thyroid gland may play an important role in carcinogenesis in the brain, principally because its hormones affect differentiation of the brain cells and tissues [9]. Changes in thyroid function in the presence of verified brain tumors have been studied extensively in clinical material [3, 5, 6, 7].

However, clinical material is difficult to interpret because observations have been made on patients with brain tumors differing in structure and localization and in the duration of their course. The results are conflicting and do not give a clear picture of the role played by these changes in thyroid function or the imbalance between thyroid hormones in the body in the development of the brain tumor. A more promising method of establishing the general principles is to simulate tumor development in the brain of animals under conditions of thyroid hormonal imbalance which can be controlled by the experimenter.

No reference could be found in the literature to studies of the effect of thyroid hormonal imbalance on growth of transplanted brain tumors.

For this purpose, strain (101/12) of a transplantable dedifferentiated cerebellar astrocytoma of rats, obtained by the writer using Yablonovskaya's method [8], has been used in the Laboratory of Histopathology of the Nervous System. During repeated transplantation the tumor underwent malignant change, and in later passages was identified as glioblastoma multiforme.\*

## EXPERIMENTAL METHOD

Experiments were carried out on 64 sexually immature noninbred female albino rats weighing 50-70 g.

Growth of the glioblastoma multiforme was studied in experimental animals with complete athyreosis resulting from total one-stage removal of both lobes of the thyroid gland, and of hypothyreosis resulting

\*L. Ya. Yablonovskaya was responsible for the histological study of the strain.

---

Laboratory of Histopathology of the Nervous System, Research Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 69, No. 3, pp. 95-97, March, 1970. Original article submitted July 21, 1969.

©1970 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.

TABLE 1. Effect of Total and Subtotal Thyroidectomy on Life Span of Rats with Transplanted Glioblastoma Multiforme

Group of animals	Number of animals	Weight of animal (in g)	Weight of reproductive organs (in mg/100 g body weight)		Life span (in days)	Statistical indices		P
			ovaries	uterus		index studied	groups compared	
I. Subtotal thyroidectomy	17	139.5±22.56	51.7±7.33	116.7±43.14	16.57±1.76	Life span (in days)	I и III	0.995
II. Total thyroidectomy	47	118.1±39.4	54.02±5.96	135.0±15.69	18.83±1.51		I и IV	0.85
III. Control, sexually mature	10	143.4±13.91	49.5±7.94	152.2±52.9	12.6±1.51		II и III	0.999
IV. Control, sexually immature animals	33	118.3±10.40	46.36±7.32	126.9±20.82	15.79±1.32		II и IV	0.95

Legend: Sd denotes error of difference, P level of probability.

from subtotoal thyroidectomy. The operation was performed 30 days before transplantation of tumor cells. The chief criterion of the rats of tumor growth was the incubation period of its development from the time of transplantation until the day of appearance of a clearly defined clinical picture of the disease or death of the animal.

The control series consisted of 43 rats into which tumor cells were transplanted without previous disturbance of the thyroid hormonal balance. Consideration was paid in these experiments to the degree of malignancy of the tumors (the serial number of passage), the time of year, changes in weight of the animals and their sexual development during the experiment, the presence of tumors in the brain of rats which died or were killed, and the completeness of removal of the thyroid glands or the degree of their regeneration. All the numerical results were subjected to statistical analysis by the usual method using a key-actuated machine of the Rheinmetall type.

## EXPERIMENTAL RESULTS

Total thyroidectomy retarded growth of the animals, which weighed 118.1±39.4 g compared with 143.4±13.91 g in the control (Table 1). In addition, subtotal and total thyroidectomy caused some delay in the sexual development of the experimental rats compared with the control sexually mature animals. While the weight of the ovaries was the same, the weight of the uterus of the experimental rats was 116.7±43.14 and 135.0±15.69 mg/100 g body weight respectively, compared with 152.2±52.9 mg/100 g body weight for the controls. Although this difference is not statistically significant, it nevertheless suggests that the hormonal functional of the ovaries was slightly depressed in the experimental rats. It has been shown experimentally [2] that castration retards growth of transplanted ependymoblastomas in mice, and in clinical neuro-oncology, the therapeutic action of estrogens [4] and the pathogenetic effects of profound hormonal disturbances such as puberty, pregnancy, and the menopause [1] on the growth of brain tumors have been observed. In view of these facts, the life span of the experimental rats was compared with that of an additional control (group IV). The actual age of these rats was less than that of the experimental animals, but the state of their reproductive systems was identical.

The life span of the subtotally thyroidectomized rats was 16.57±1.76 days. The control sexually mature rats lived 12.6±1.51 days, and the sexually immature rats lived 15.79±1.32 days. Calculation of the mean values showed that subtotal thyroidectomy retards growth of the tumor and death of the animals compared with their course in sexually mature rats (P=0.995) but does not affect rate of growth of tumor by comparison with the control, including the group of sexually immature rats (P=0.85). Total thyroidectomy (life span 18.83±1.51 days) inhibited growth of the tumor and retarded death of the rats by comparison with both controls. The level of significance was 0.95-0.99.

The results thus show that hypothyreosis and, in particular, athyreosis in rats prolongs the latent period of the disease and retards the death of rats with transplanted cerebellar glioblastoma multiforme.

# LITERATURE CITED

1. A. P. Avtsyn, Arkh. Pat., No. 12, 3 (1963).
2. A. P. Avtsyn and L. Ya. Yablonovskaya, Proceedings of the 8th International Cancer Congress [in Russian], Vol. 3, Moscow - Leningrad (1963), p. 478.
3. Ya. M. Buntser, State of Thyroid Function during Brain Tumors, Candidate's Dissertation [in Russian], Khar'kov (1964).
4. I. N. Vinogradova, in: Physiological Basis of Neurosurgical Operations [in Russian], Moscow (1954), p. 165.
5. I. D. Virozub, in: Problems in Surgery [in Russian], Vol. 3, Kiev (1957), p. 211.
6. L. S. Gitkina, Proceedings of a Conference of Junior Neurosurgeons [in Russian], Moscow (1960), p. 15.
7. D. G. Palinkashi, The Method of Whole-Body Radiometry in the Investigation of Iodine Metabolism and Its Application to Clinical Neuro-oncology, Candidate's Dissertation [in Russian], Moscow (1966).
8. L. Ya. Yablonovskaya, Experimental Brain Tumors Produced by Heterotransplantation and Induction [in Russian], Leningrad (1967).
9. I. T. Eayrs, in: Brain-Thyroid Relationships with Special Reference to Thyroid Disorders, London (1964).