INCORPORATION OF RADIOACTIVE PHOSPHORUS IN HEART MUSCLE OF RATS WITH IMPLANTED BRAIN TUMORS IN VARIOUS STAGES OF DEVELOPMENT

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The chemical changes in the heart muscle during growth and development of cerebral neoplasms has not yet been studied, although facts have been reported indicating the appearance of functional disturbances of varied character in heart muscle in association with pathological processes of this nature [1, 4]. No investigations have been made of metabolism in heart muscle at various stages of growth of cerebral tumors, probably on account of the lack of an adequate biological model. Accordingly, the study of the phosphorus metabolism is of considerable interest, for this element is a component of a highly important group of biological compounds concerned in all forms of metabolism and, in particular, in the processes of accumulation and dissipation of energy.

In the present investigation an attempt was made to study the incorporation of P^{32} into the phosphorus-containing fractions of heart muscle, which are of great importance in the mechanisms of its metabolism and function [2, 5, 6, 7].

EXPERIMENTAL METHOD

Investigations were conducted on noninbred male albino rats weighing 100-130 g, kept in ordinary conditions and on a normal diet. The animals were divided into 4 groups, of which 3 (each consisting of 5 rats) were experimental and one (6 rats) was a control. As a first step a glial type of tumor of strain T-9 (an ependymoblastoma supplied by I. N. Dimant) was implanted into the brain of the experimental rats.

Four hours before sacrifice the rats received an intraperitoneal injection of radioactive phosphorus in the form

Intensity of Incorporation of P^{32} into Heart Muscle at Various Stages of Development of a Tumor Implanted into the Brain

Period of development of tumor (in days)	Radioactivity of total phosphorus (as % of control)						Radioactivity of phosphorus-containing fractions (as % of control)					
	total blood phosphorus	t	total phosphorus of heart muscle	t	phospholipids	t	Phosphorus-containing acid-soluble fractions	t	nucleic acids	t	phosphoproteins	t
5	83,2	3,1	284,1	4,8	391,2	34	23,56	41	74,04	3,2	62,34	4,5
10	32,0	19,4	80,24	5,1	59,06	5,4	111,6	6,1	57,73	4,6	68,61	5,0
14—15	28,0	18,3	66,24	8,6	30,91	8,9	117,3	5,5	108,6	1,0	41,42	7,8
Control	100		100		100		100		100		100	

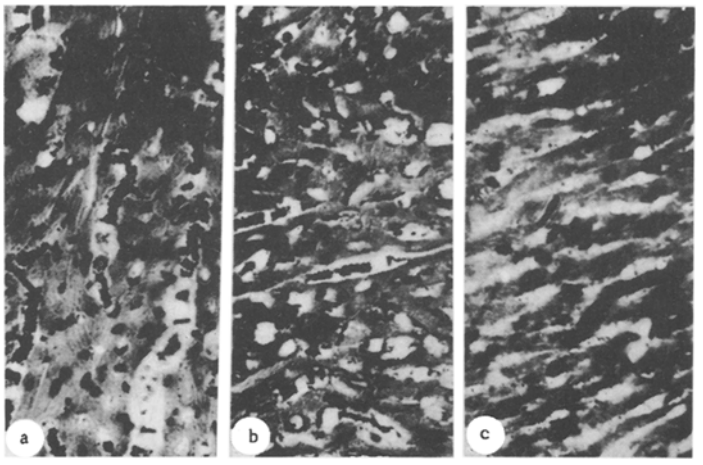

Fig. 1. Histoautoradiograms of muscle of the left ventricle of the heart of rats with transplanted brain tumors. a) 5th day of development of implant; b) 10th day; c) 15th day. Hematoxylin-eosin. Magnification 40 × 10.

of $Na_2HP^{32}O_4$ in a dose of 1 μ Ci/g body weight. The animals were sacrificed by decapitation: the rats of group 1 on the 5th day, group 2 on the 10th day, group 3 on the 14th-15th day (the day when signs of a circumscribed brain lesion first appeared). After sacrifice, the heart was carefully freed from blood by washing. Part of the organ (an area of the myocardium of the left ventricle) was taken for radiometric investigation, and the rest was fixed in Carnoy's fluid and subjected to histoautoradiographic investigation.

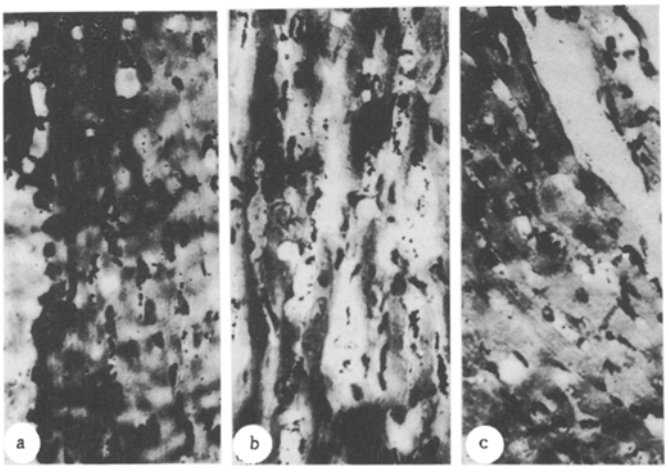

Fig. 2. Histoautoradiogram of different areas of heart muscle of left ventricle of a rat with a tumor implanted into the brain, on the 10th day after implantation. a) Region lying next to endocardium; b) middle layer; c) region lying next to epicardium. Hematoxylin-eosin. Magnification 40 × 10.

Studies were made of the radioactivity of the total phosphorus, the incorporation of P^{32} into the phospholipids, the phosphorus-containing part of the acid-soluble fractions, the nucleic acids, and phosphoproteins. The incorporation of P^{32} was determined by Grakhovet's method, as modified by Sorokin and Ioffe [3]. The number of impulses was determined by means of a type B-2 apparatus with an MST-17 end-type counter. The radioactivity of the targets was estimated per 100 mg fresh tissue. The results showing the incorporation of P^{32} into the phosphorus-contain-

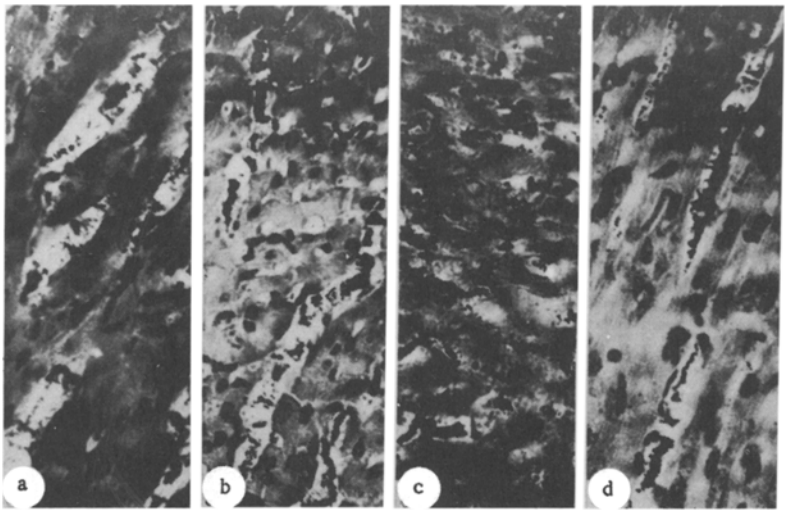

Fig. 3. Histoautoradiogram of different portions of heart muscle of a rat with tumor implanted into the brain, on the 5th day after implantation. a) Right ventricle; b) left ventricle; c) right atrium; d) left atrium. Hematoxylin-eosin. Magnification 40 × 10.

ing fractions were calculated as percentages of the radioactivity of the total phosphorus, and expressed as percentages of the activity of the corresponding fractions in the control animals. The numerical results were analyzed by statistical methods.

For contact histoautoradiography sections of the heart were cut, stained with hematoxylin-eosin, and covered with type P (NIKFI) liquid nuclear emulsion in dilution of 1:4-1:6. The time of exposure was determined experimentally and amounted to 25 days.

EXPERIMENTAL RESULTS

It is clear from the results given in the table that on the 5th day of growth of the tumor the intensity of incorporation of P^{32} into the heart muscle had increased to almost 3 times the control value. The distribution of P^{32} in the phosphorus-containing fractions also showed changes: the radioactivity of the phospholipids had increased, while the intensity of incorporation of P^{32} into the acid-soluble phosphorus-containing fractions, nucleic acids, and phosphoproteins showed a decrease. On the 10th day of the experiment a decrease in the accumulation of the isotope in the heart muscle was observed. The activity of all the phosphorus -containing fractions showed a parallel fall, apart from the acid-soluble compounds, which showed the opposite tendency. During the period of marked clinical manifestations of tumor growth (on the 14th-15th day) a further decrease was observed both in the total radioactivity and in the intensity of incorporation of P^{32} into the phospholipids and phosphoproteins, while the P^{32} concentration in the acid-soluble fractions continued to rise. The indices of P^{32} incorporation into the nucleic acids showed no significant difference.

On the tracer autoradiograms of the heart muscle of rats sacrificed on the 5th day after transplantation of the tumor, the number of tracks of β -particles from P^{32} was significantly greater than in the control and at all other times of the experiment; a progressive fall in the intensity of incorporation of the indicator was seen on the 10th and 14th-15th days of the experiment (Fig. 1).

The longitudinal and transverse sections of the heart muscle show that the radioactive tracer was mainly present in the intermuscular spaces, especially in the middle part of the myocardium. The intensity of incorporation of P^{32} was lower in areas situated near the endocardium and epicardium (Fig. 2). A definite regularity of distribution of the isotope was also observed in the various portions of the heart: high intensity of incorporation was usually observed in the muscle of the left ventricle, and then followed the right ventricle, and the left and right atria (Fig. 3). The changes described above, characterizing the incorporation of P^{32} into the tissue structures of the heart in rats with transplanted brain tumors, developed parallel with the development of the neoplastic process in the brain.

The results described indicate that in the early stages of development of a tumor implanted into the brain the intensity of incorporation of P^{32} into the heart muscle rose distinctly; this fact evidently demonstrates the intensification of metabolic processes and an increase in the expenditure of energy in the myocardium. Later, on account of progressive growth of the neoplasm, the intensity of incorporation of P^{32} into the tissue structures of the heart was disturbed to an even greater degree, but in the direction of a decrease. It may be supposed that this was due to a disturbance of the metabolic processes in the heart muscle on account of toxic influences from the malignant focus, and to its direct action on the regulatory centers of the pituitary–hypothalamic region.

This connection between the changes described above and metabolic processes, and,to an even greater degree, with the character of the circulation of the blood in the heart muscle, was confirmed by a comparative study of the accumulation of P^{32} in the blood and heart at the same periods of investigation (see table).

The pathological changes observed in the dynamics of the phosphorus metabolism in the heart muscle of the experimental animals with implanted brain tumors correspond to electrophysiological findings reflecting the changes in its functional state in the presence of a malignant tumor affecting the central nervous system. This conclusion is confirmed by clinical observations [1, 4], and we have also confirmed it experimentally.

SUMMARY

The character of radiophosphorus incorporation into the phosphorus-containing fraction of the cardiac muscle was studied during various stages of the development of transplanted glial tumors in rats. An intensified P^{32} accumulation was ascertained radiometrically in the cardiac muscle at the initial period (the 5th day) of development of the tumor implant chiefly at the expense of its incorporation into the phospholipids. Later, on the 10th and 14th-15th days of tumor development, there was a progressive reduction in P^{32} content in the cardiac muscle and in its phosphorus-containing fractions, with some rise in the intensity of P^{32} incorporation into the acid soluble fractions.

The results of histoautoradiographic investigations corresponded to the radiometric findings.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
