EFFECT OF SUBCUTANEOUS TRANSPLANTATION OF SARCOMA SSK ON AUTOPROTEOLYTIC ACTIVITY OF RATS' BLOOD

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An increase in the autoproteolytic activity of the blood was found in rats with a transplanted sarcoma SSK. This phenomenon has previously been found in patients with carcinoma of the uterus.

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Our previous investigation [2] showed that the autoproteolytic activity of the blood of patients with carcinoma of the cervix uteri is on the average twice as high as that in healthy women, women with benign tumors of the reproductive organs, and patients with various inflammatory diseases. The greatest increase in proteolysis was found in stage II and, in particular, in stage I. Subsequently this fact was also established for carcinoma of the body of the uterus. This phenomenon is interesting both from the point of view of its practical use as a method of early diagnosis, and also in connection with the study of some aspects of malignant growth.

In the present investigation an attempt was made to discover whether the phenomenon of increased autoproteolytic activity is characteristic of malignant tumors in the situations mentioned, or whether it is also found in processes affecting other organs and systems. To examine this problem we used a transplanted tumor.

EXPERIMENTAL METHOD

Experiments were carried out on 70 noninbred female albino rats weighing 140-150 g. The initial blood autoproteolytic activity was determined in all the animals. Blood for investigation was taken from the amputated tip of the tail. Autoproteolytic activity was measured from the increase in nonprotein nitrogen in the sample following incubation for 24 h at 37° with inactivation of antiproteases [2]. The result was expressed as increase in nonprotein nitrogen (in mg%).

TABLE 1. Increase in Autoproteolytic Activity of Blood of Experimental Rats After Transplantation of Sarcoma SSK (statistically analyzed difference of activity between results on specified day after transplantation and initial value)

	Day of investigation after transplantation			
	9-12	20-24	28-29	35-36
Number of experimental rats	52	52	40*	70*
Increase in autoproteolytic activity compared with initial level (together with standard error in mg%)	38 ± 3	21 ± 5	13 ± 4	10 ± 3

*Remaining animals had died by this time.

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Ten animals were kept as controls; throughout the experiment their proteolytic activity was determined periodically. The remaining 60 rats were inoculated subcutaneously with sarcoma SSK. This tumor is marked by a high rate of successful transplantation and by high malignancy, so that the experiment can be performed quickly and demonstrable results obtained. Periodically during growth of the tumor, blood was taken from all the rats for investigation. For various technical reasons, eight experimental animals were withdrawn from the experiment.

EXPERIMENTAL RESULTS

Examination of the control animals showed that the changes in autoproteolytic activity of the blood during the experiment were negligeable (on the average from 19.6 to 22.8 mg%).

A different picture was observed in the animals on the experimental group. On the 9th-12th day after transplantation of the tumor, the autoproteolytic activity increased in all the rats. Thereafter it remained above its initial level, although it fell steadily from the level of its activity on the 9th-12th day. Statistically analyzed indices of the increase in blood proteolytic activity of the rats compared with its initial level are given in Table 1.

It is clear from Table 1 that the changes in autoproteolytic activity of the rats' blood during growth of sarcoma SSK are identical with the changes in this index in patients with carcinoma of the cervix and body of the uterus [2]: in both cases a sharp increase in proteolysis is observed in the initial stages of the disease, with a gradual decrease in the course of development of the malignant tumor, although not reaching the values characteristic of a healthy state. This suggests that the phenomenon under investigation is characteristic of malignant growth in general, irrespective of the localization of the process and the species of host carrying the tumor. More extensive investigations are needed before this problem can be finally solved.

The simplest explanation of the changes discovered in proteolytic activity may be the activation of the defensive powers of the body, aimed at eradication of the invading tumor. It may be postulated that during development of a malignant process these defensive powers are inhibited (or extinguished), and this is reflected by the subsequent decrease in activity.

To judge from the evidence obtained in some investigations [1, 3], changes similar to those which we found in the case of autoproteolytic activity are also observed in connection with the desoxyribonuclease activity of the blood serum. Although absent under normal conditions, desoxyribonuclease activity is observed in the serum in most patients with stage I of carcinoma; in stages II and III of carcinoma this activity is increased in approximately 50% of patients, while in stage IV as a rule it is absent. Proteolytic enzymes and nucleases belong to a group of hydrolytic enzymes many of which are present in lysosomes. On this basis a different hypothesis from that given earlier may be put forward, namely that there is a sharp increase in permeability of lysosome membranes in the initial stage of tumor development, followed by a graudal decrease in their permeability (or exhaustion of the contents of the lysosomes) in the course of growth of the tumor.

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