CHANGES IN THE CONTENT OF BLOOD THROMBOKINASE AND FIBRINOGEN IN THE PROCESS OF GROWTH OF A TRANSPLANTED SARCOMA

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Certain facts have been described in the literature concerning the interrelation between changes in the blood coagulation components and tumor growth. Thus, Keil [7] cites the data on the rise of the coagulability of the blood and the fibrinogen content of the blood of patients suffering from malignant tumors. Clifton and Grossi [5] indicate the enhanced thromboplastic activity of certain tumor tissues. In this connection, of interest are observations by Fischer [6] in regard to the accelerated cellular growth in tissue dultures parallel with an increased content of thrombokinase in them. In recent years, the data of M. A. Ukolova and G. A. Leont'eva [4] were published regarding the high content of thrombokinase in the tissue culture of a 45 and M-1 rat sarcoma, as well as in human cancer tissues.

In order to study further the problem of the interrelation between tumor growth and the blood coagulation components we undertook an investigation of the fibrinogen content of the blood and of the thrombokinase activity of the blood in animals during the growth process of transplanted experimental tumors.

METHOD

Experiments were carried out on white male rats weighing 120-150 gm. We used the M-1 and 45 strains of sarcoma as the most thoroughly investigated native models of rat tumors.

The blood was obtained from the jugular vein [3]. The thromboplastic activity of the blood was determined according to the B. A. Kudryashev and P. D. Ulitina method [2], but as a reagent on thrombokinase we used the plasma of rabbit's blood containing a large amount of prothrombin. The rabbit blood was obtained from the heart. Blood fibrinogen was determined according to the colorimetric method [1] based on the biuret reaction, with one difference: instead of the Pulfrich photometer we employed the photoelectrocolorimeter.

TABLE 1. Thrombokinase Activity and Fibrinogen Content in the Blood of Control Animals and in Tumor-aflicted Animals

Statistical index	Thrombokinase activity in the animals			Content of fibrinogen in the animals		
	controls	with sarcoma 45	with sarcoma M-1	controls	with sarcoma 45	with sarcoma M-1
Number of observations	20	11	62	20	11	57
Arithmetical mean	90	59	54	340	820	920
Mean-square deviation	9.3	1.9	12.3	7	160	380
Variability coefficient	10.3	3.2	22.7	20	19	40
Standard deviation	2.1	0.6	1.5	16	52	7.5
Standard deviation difference	-	2.1	2.5	-	51.6	58
Ratio $\frac{\text{mean differences}}{\text{standard deviation difference}}$	-	14.4	14.0	-	9.3	10.0

RESULTS

Two series of experiments were carried out.

In the first series, 62 animals with M-1 sarcoma, 11 - with sarcoma 45 within 2-3 weeks following transplantation of the tumors, and 20 control animals were under observation.

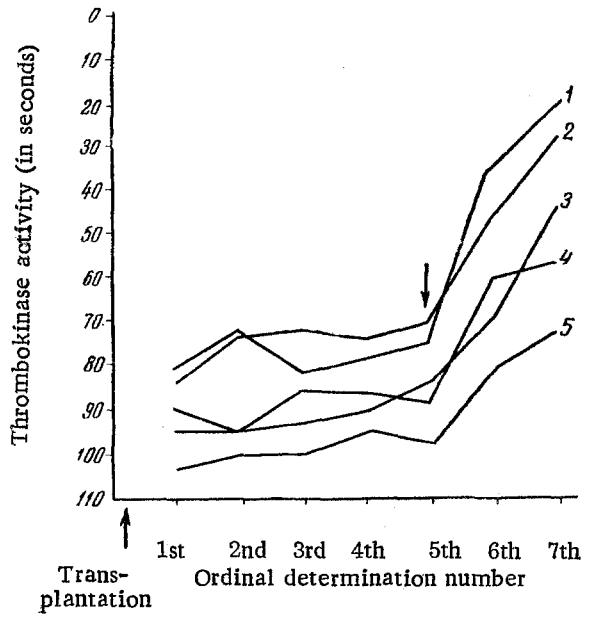

Fig. 1. The thrombokinase activity of the blood prior and after the transplantation of M-1 sarcoma in five experimental rats (1,2,3,4,5).

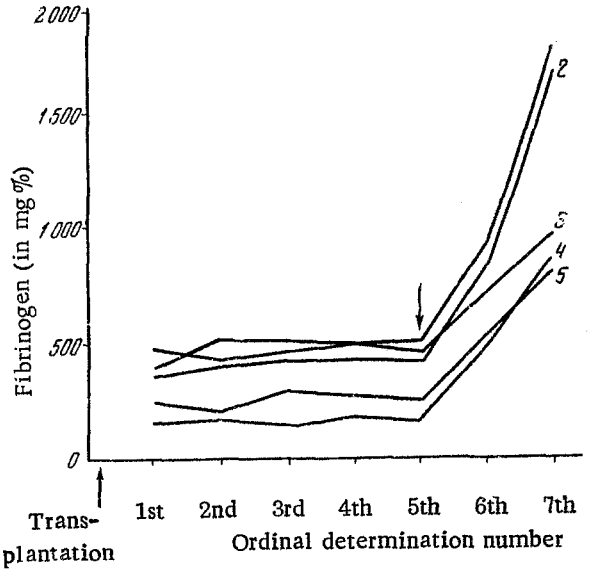

Fig. 2. Fibrinogen content of the blood prior and after the transplantation of M-1 sarcoma in five experimental rats (1,2,3,4,5).

As a result of these investigations, it was found that the fibrinogen content and the thrombokinase activity of the blood of experimental animals are considerably higher when compared to control. The rise in thrombokinase activity was manifested in the acceleration of coagulation to 54-59 seconds instead of 90 sec in controls. The fibrinogen content rose to 820-920 mg%(as compared to 340 mg%). At the same time, in control animals and especially in the experimental animals considerable fluctuations of the fibrinogen content and thrombokinase activity have taken place, as reflected by the high coefficient of variability. However, the differences in the fibrinogen content and thrombokinase activity, as observed in the tumor-afflicted animals and in the controls, are very considerable and proved to be statistically reliable (Table 1).

In the second series of experiments we observed 30 animals afflicted with tumors. Since no appreciable difference has been observed in the first series of experiments in the content of investigated components in rats with various transplanted sarcomas, we used in the second series the M-1 sarcoma strain only.

The blood examination for fibrinogen content and thrombokinase activity was carried out in 20 rats, upon the emergence of the tumor (on the 5th-6th day after the transplantation) and during the subsequent periods of its development (on the 20th-25th day). The 20 control animals were observed simultaneously. In the remaining ten rats the thrombokinase activity (five rats) and fibrinogen content (five rats) were determined during the early and latter stages of development and also for a period of five weeks prior to inoculation (Fig. 1 and 2).

The tests showed that an increase of the fibrinogen content and thrombokinase activity of the blood takes place at the very beginning of the tumor growth. As the tumor growth progressed, these changes became more pronounced (Table 2; see also Fig. 1 and 2).

The obtained results attest to the fact that the tumor development in the animal organism causes a regular increase in the coagulation factors of the blood, fibrinogen and thrombokinase in particular.

In comparing the obtained data with the data relating to the high content of thrombokinase in the investigated tumors [4], we may assume that the blood is the supplier of thrombokinase and fibrinogen to the tumor.

TABLE 2. The Thrombokinase Activity and Fibrinogen Content of the Blood in Animals During the Process of Tumor Growth

Statistical index	Thrombokinase activity in animals			Fibrinogen content in animals		
		with M-1 sarcoma			with M-1 sarcoma	
Number of observations	20	20	20	20	20	20
Arithmetical mean	90	58	39	340 mg	710 mg	1320 mg
Mean-square deviation	9.3	11.6	13.4	70	185	490
Variability coefficient	10	20	33	20	26	37
Standard deviation	2.1	2.6	3.0	16	42	110
Standard deviation difference	-	3.4	3.9	-	40	115
Ratio $\frac{\text{mean difference}^1}{\text{standard deviation difference}}$	-	9.7	13	-	8.6	8.5

[1]Required ratio magnitude equals 3

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