ADENOSINE DEAMINASE ACTIVITY IN HEPATOMAS OF DIFFERENT DEGREES OF MALIGNANCY

S. Ya. Davydova and S. S. Vetchinin

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The adenosine deaminase activity in tumors with a high degree of malignancy, namely Gel'shtein's ascites hepatoma 22 and Ehrlich's ascites carcinoma, was reduced to one-third of that in normal liver. In hepatomas with a low and average degree of malignancy, activity of the enzyme was reduced by only 20%. Some decrease in enzyme activity also was found in the liver of mice with tumors.

KEY WORDS: adenosine deaminase; ascites hepatoma 22 and Ehrlich's ascites carcinoma; degree of malignancy.

Adenosine deaminase is a widely distributed enzyme but its role in metabolism has received little study, possibly because it takes part in several catabolic processes. The special interest in this enzyme is connected with observations which showed correlation between adenosine deaminase deficiency in lymphocytes and deficiency of the immune system of the body [3]. Adenosine deaminase activity is widely investigated in clinical practice as a relative index of the integrity of immune reactivity in various types of malignant disease.

In this investigation adenosine deaminase activity was studied in transplantable tumors with different degrees of malignancy and compared with that in normal liver and in the liver of animals with tumors.

EXPERIMENTAL METHOD

Noninbred albino mice were inoculated with Ehrlich's ascites carcinoma and C3HA mice with Gel'shtein's transplantable hepatomas [1]. Among the tumors studied were the most rapidly growing and most malignant strain hepatoma 22 (ascites variant, the hepatoma appears 5-7 days after inoculation, maximal period of survival of mice with the tumor 1 month), slowly growing hepatoma 60 (appears 1 month after inoculation, survival period of animals with the tumor 1 month), and hepatoma 61 (develops 1-1.5 months after inoculation, survival period of these mice 1.5 months). Hepatomas 60 and 61 are of an average degree of malignancy. Hepatoma 46 grows more slowly still (it appears 1.5 months after inoculation and the survival period of the mice with the tumor is over 1 year). Hepatoma 46 is the least malignant of those tested. Ehrlich's ascites carcinoma appears 5-7 days after inoculation and the survival period of these animals does not exceed 1 month.

Adenosine deaminase activity was determined in the supernatant obtained after centrifugation of a tissue homogenate [4, 5] in 0.01 M Tris-HCl, pH 8.0, for 20 min at 11,000g. The determination was based on the decrease in optical density (E) during deamination of adenosine to inosine, measured at 265 nm. To 10 μl of supernatant 2 ml of 36 μM adenosine in 0.1 M Na-phosphate buffer, pH 7.0, was added. The mixture was incubated for 30 min at 37°C and the reaction stopped by the addition of 1 ml of 0.1 M HCl. HCl was added to the control samples before incubation. Standard mixtures containing 36 μm adenosine and inosine in proportions of 2:0, 3:1, 1:1, 1:3, and 0:2 respectively were prepared. A calibration curve of E_{265} against the ratio of adenosine to inosine was plotted.

EXPERIMENTAL RESULTS

The results of investigation of adenosine deaminase activity in the various tumors and in the liver of the animals with tumors, compared with its activity in normal mouse liver are given in Table 1.

As Table 1 shows, adenosine deaminase activity in hepatomas with low and average degrees of malignancy (hepatomas 46, 61, and 60) did not differ significantly from normal, being reduced on average by 20%. It is

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TABLE 1. Adenosine Deaminase Activity (in nmoles adenosine/mg protein/min) in Tumors with Different Degrees of Malignancy and in Liver (M ± m)

Liver of C3HA mice	Hepatoma								Liver of non-inbred mice	Ehrlich's carcinoma	
	46		61		60		22				
	L	H	L	H	L	H	L	H		L	C
6,69± ±1,15	4,94± ±1,67	5,06± ±0,95	5,8± ±1,17	5,8± ±1,13	5,98± ±0,86	6,28± ±0,51	5,48± ±0,87	2,64± ±1,25	5.7± ±0.18	6,89± ±0,42	1,94± ±0,8

Legend. L) Liver, H) hepatoma, C) carcinoma.

interesting to note that in the liver of mice with tumors, just as in the tumors themselves, the activity of this enzyme was somewhat low.

A clear decrease in adenosine deaminase activity was found in tumors with a high degree of malignancy: hepatoma 22 and Ehrlich's ascites carcinoma. The activity of the enzyme was reduced by two-thirds in these tumors. In this case also, the enzyme activity in the liver of animals with hepatoma 22 also was lower, though not significantly, than in the liver of normal mice.

Straub [2] found a marked decrease in adenosine deaminase activity in Ehrlich's ascites cells [2]. Increased activity of the enzyme was found in that investigation also in the ascites fluid and in the blood plasma of persons with various tumors. In solid tumors and acute lymphatic leukemia the adenosine deaminase activity in the lymphocytes of the patients was sharply reduced.

During the growth of a tumor the metabolism and content of purines are evidently disturbed in the tissues of the host organism. The increased level of purine compounds, especially adenosine, in the lymphocytes can, it can tentatively be suggested, lead to depression of the immune response aimed against the tumor antigens in the malignant cells [6].

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