LACTATE DEHYDROGENASE ISOZYME SPECTRUM IN MOUSE MAMMARY GLAND TUMORS AND METASTASES IN THE LUNGS

I. P. Tereshchenko, V. I. Boikova, and I. S. Zaretskaya

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The lactate dehydrogenase isozyme spectrum was investigated in the mammary glands, lungs, spontaneous mammary gland tumors, and metastases of tumors in the lungs of female mice of the high-cancer strain C3H previously having given birth to young. Differences in the isozyme spectrum of the metastases and tumors were reflected in the larger fractions migrating to the anode in the metastatic nodes. The presence of a metastasis in the lung was accompanied by a cathodal shift in the isozyme spectrum of the lung tissues.

KEY WORDS: lactate dehydrogenase; isozymes; mammary gland tumors; metastases in the lung.

The isozyme spectrum of lactate dehydrogenase (LD) in tumors is known to differ from that of normal tissues by an increase in the activity of the cathodal fractions of the enzyme [1, 3, 6]. So far as the state of the LD isozyme spectrum in metastases is concerned, information in the literature is very limited in quantity and contradictory in nature. Some workers have found a decrease in the activity of anodal fractions in metastases of a transplanted tumor compared with the tumor tissue itself [2, 5, 9], whereas others found no difference between the isozyme spectra of the tumor and its metastases [7, 8]. To understand the mechanisms of metastasization it is particularly interesting to study spontaneous tumors in animals, for these bear the closest resemblance to human pathology.

The object of this investigation was to study the LD isozyme spectrum, using spontaneous mouse mammary gland carcinoma as the model, not only in the primary tumors and metastases, but also in the tissues of the organ where the metastases appeared. The gathering of information in this field will give a deeper insight into the role of metabolic processes in metastasization.

EXPERIMENTAL METHOD

Experiments were carried out on female C3H mice, over 1 year old, which had produced young. The following groups were distinguished: 1) intact females with no visible sign of a tumor, 2) females with a tumor, and 3) females with tumors and metastases. The mammary glands, lungs, mammary gland tumors, and metastases of the tumors in the lungs were investigated biochemically. The LD isozyme spectrum was determined by Wieme's method in the modification in [4]. A parallel morphological analysis of the material was made. Paraffin sections of the organs were stained with hematoxylin–eosin.

EXPERIMENTAL RESULTS AND DISCUSSION

The investigations showed that the LD isozyme spectrum in the mammary glands of intact animals was characterized by predominance of the cathodal fractions, especially LD_5, a fact that is linked with the intensive synthesis of M-subunits. Evidence for it is given by the

Laboratory of Pathophysiology, P. A. Gertsen Oncological Research Institute, Moscow.
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TABLE 1. LD Isozyme Spectrum in Tissues of Mice

Tissues studied	Number of animals	LD isozymes, in % (M ± m)					$\frac{LD_5}{LD_1}$	$\frac{\Sigma M}{\Sigma H}$
		1	2	3	4	5		
Mammary glands of intact animals	18	7,7±0,7	10,3±0,6	18,5±1,2	17,8±1,6	41,3±1,9	5,4	2,5
Mammary gland tumors	9	2,8±0,3	6,3±0,7	15,3±0,9	23,9±1,5	49,9±1,9	17,5	3,7
Mammary glands of animals with tumors	16	4,4±0,5	8,7±0,8	16,2±0,8	22,1±1,2	47,7±1,0	10,8	3,0
Mammary gland tumors in animals with metastases	9	0,4±0,02	5,6±1,1	15,3±3,3	30,6±1,8	50,2±2,8	125,5	4,1
Mammary glands of animals with tumors and metastases	9	3,4±0,7	8,8±0,4	17,7±1,3	27,1±2,0	47,0±1,2	14,0	3,1
Metastases of mammary gland tumors in the lungs	9	5,2±1,4	12,3±1,7	15,4±1,1	17,7±1,3	45,7±2,8	8,8	2,6
Lungs of intact animals	13	9,7±0,8	15,0±1,2	20,6±1,3	10,9±0,6	41,8±3,1	4,2	1,9
Lungs of animals with tumors	19	11,0±0,8	16,1±1,2	17,2±0,8	14,0±0,9	41,8±2,0	3,8	2,2
Lungs of animals with tumors and metastases	9	8,3±0,6	12,1±1,1	14,2±1,0	18,5±2,2	44,3±2,7	5,3	2,4

values of the coefficient $\Sigma M/\Sigma H$ (2.5) and the ratio LD_5/LD_1 (5.4; Table 1). An increase in synthesis of M-subunits and a decrease in the activity of the anodal fractions were observed in mammary gland tumors, as reflected not only by an increase in the $\Sigma M/\Sigma H$ coefficient to 3.7 but also by a considerable increase in the LD_5/LD_1 ratio (to more than three times its value in the intact animals). To assess any possible pretumor changes in the potentially tumor-bearing animals the LD isozyme spectrum in the mammary glands was studied in the absence of any visible neoplastic lesion. According to the indices of activity of the LD fractions they were found to occupy an intermediate position between tumors and the mammary glands of intact mice (Table 1).

In mice with metastases the most characteristic feature of the isozyme spectrum of the primary tumor focus was a sharp decrease, or sometimes the total absence, of LD_1. A tendency was observed for the synthesis of M-subunits to increase further both in the tumor itself and in the opposite mammary glands in which no signs of neoplastic lesions could be seen. As regards metastases, their isozyme spectrum differed from that of the primary tumor in having larger anodal fractions ($\Sigma M/\Sigma H = 2.6$ compared with 4.1 in the tumors; $P < 0.001$). Meanwhile in the cathodal zone there was a marked decrease in LD_4 activity (17.7 compared with 30.6 in the tumors; $P < 0.001$).

In the intact animals the LD isozyme spectrum of the lung (the organ most commonly affected by metastases) was distinguished by high LD_5 activity and also by a considerable LD_3 value, characteristic of that organ. The appearance of a tumor in the body was accompanied by some redistribution of the enzyme activity among its fractions in the lung tissue: Activity of LD_4 was increased and that of LD_3 was reduced ($P < 0.001$). The appearance of metastases in the lungs caused a marked decrease in LD_3 activity and also a marked cathodal shift, caused by an increase in synthesis of M-subunits ($\Sigma M/\Sigma H = 2.4$ compared with the normal 1.9; $P < 0.001$).

The development of spontaneous mammary gland tumors in mice is thus accompanied by changes in the LD isozyme spectrum in the direction of increased activity of the cathodal fractions. The isozyme spectrum of metastases in the lungs is characterized by indices reflecting the distinctive isozyme spectrum of that organ, as shown by the higher activity of the anodal fractions in the metastases than in the tumors. The presence of metastases in the lungs is accompanied by a cathodal shift of the LD isozyme spectrum in the tissues of that organ, i.e., the spectrum changes in the typical direction for the primary tumor focus.

LITERATURE CITED

1. É. G. Gorozhanskaya and V. S. Shapot, Vestn. Akad. Med. Nauk SSSR, No. 3, 28 (1971).
2. B. M. Zel'vin, N. I. Bolonina, and I. P. Tereshchenko, Vopr. Onkol., No. 4, 76 (1974).

3. V. S. Shapot, Zh. Vses. Khim. Ova., 15, No. 6, 690 (1970).
4. Yu. A. Yurkov and V. V. Alatyrtsov, Lab. Delo, No. 12, 705 (1966).
5. L. Cirnu, V. Lengyel, Z. Lengyel, et al., Bull. Cancer, 55, 517 (1968).
6. R. D. Goldman, N. O. Kaplan, and T. C. Hall, Cancer Res., 24, 389 (1964).
7. W. Küstner and J. Weinreich, Klin. Wschr., 48, 560 (1970).
8. G. Pfleiderer and E. D. Wachsmuth, Biochem. Z., 334, 185 (1961).
9. A. L. Sherwin, F. E. Le Blanc, et al., Arch. Neurol. (Chicago), 18, 311 (1968).