Lipid Spectrum of Erythrocyte Membranes in Cancer Patients

V. V. Novitskii, E. A. Stepovaya, N. G. Bazhenova, V. E. Gol'dberg, M. V. Kolosova, E. V. Saprykina, E. A. Gubert, I. B. Sokolova, K. G. Koreshkova, and Ya. V. Bulavina

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 126, No. 8, pp. 204-206, August, 1998
Original article submitted February 3, 1998

In patients with untreated tumors (lung cancer, head and neck tumors, stomach and colon cancer), erythrocyte membranes are characterized by a decreased content of total lipids together with increased percentage of cholesterol and lysophosphatidylcholine in comparison with healthy individuals. The observed shifts depend on tumor location.

Key Words: *erythrocyte; lipids; lung cancer; head and neck tumors; stomach cancer; colon cancer*

Neoplastic processes are always accompanied by more or less pronounced changes in the erythroid stem cells [6,10,15]. Disturbances in the erythron against the background of neoplastic transformation result in decompensation of erythropoiesis and alter erythrocyte membrane function and blood microrheology thus aggravating tissue hypoxia and impairing the patient's condition [1,4]. In light of this, erythrocyte membranes are the universal object for evaluating the intensity of membrane-destabilizing processes [8]. An important role belons to by pathochemical characteristics of cell membranes: the state of cation-transporting systems, structural and functional rearrangements in membranes and intensity of lipid peroxidation and lipid metabolism [3,5]. The aim of the present study was to investigate the lipid spectrum of the erythrocyte plasma membrane in patients with various malignant neoplasms (lung cancer, head and neck tumors, stomach and colon cancer).

Institute of Pharmacology, Institute of Oncology, Tomsk Research Center, Siberian Division of the Russian Academy of Medical Sciences, Siberian State Medical University, Tomsk

MATERIALS AND METHODS

We examined 94 patients (80 men and 14 women) aged 44-69. There were practically no differences in the measured parameters (total content and composition of the erythrocyte plasma membrane lipids) between men and women in cancer patients and healthy donors. Experimental group comprised 34 patients with lung cancer, 27 patients with neck and head tumors, 19 patients with stomach cancer, and 14 patients with colon cancer. The diagnosis was verified by X-ray, morphological, and endoscopic examinations. Experiments were carried out before the start of antitumor therapy. The control group comprised 24 healthy donors. Blood was drawn after a 10-12-h fasting period. For each patient, the total content [12,13] and composition [9] of the erythrocyte membrane lipids were analyzed.

Lipids were extracted as described elsewhere [14] and analyzed by thin-layer chromatography using Sorbfil plates (Russia); phospholipids were fractionated on Silufos-UV-254 (Czech Republic). Neutral lipids were separated in a heptan:diethyl ether:ethylacetate system (80:20:1.5), phospholipids were fractionated in a chloroform:methanol:water

0007-4888/98/0008-0823$20.00

TABLE 1. The Total Content and Composition of the Erythrocyte Membrane Lipids in Tumor Patients (*M±m*)

Group	Total lipid, g/liter	Total phospholipids, %	CH, %	Triglycerides, %	CH esters, %
Healthy donors	3.57±0.10	23.21±0.94	33.75±0.88	19.32±1.44	23.72±1.74
Lung cancer	3.14±0.11**	20.85±1.43	40.36±1.69**	15.20±1.27*	23.58±1.67
Neck and head tumors	3.02±0.14**	20.15±1.43	36.19±1.62	19.38±1.21*	24.28±1.84
Stomach cancer	2.69±0.20***x	20.00±1.83	39.41±1.57**	18.21±1.01	22.34±1.35
Colon cancer	2.94±0.16x	22.83±1.76	41.12±3.70x	16.00±1.39	20.06±3.00

Note. Here and in Table 2: *$p<0.05$, **$p<0.01$, ***$p<0.001$, *$p<0.02$ compared with healthy donors, *$p<0.05$ compared with lung cancer.

system (32:12.5:2). Spots were identified using Sigma standards. The data were processed statistically using the Student *t* test (for normal distribution) or nonparametric tests.

RESULTS

A considerable decrease in total lipid content of erythrocyte membranes was revealed in tumor patients in comparison with donors (Table 1). In patients with stomach cancer, this parameter was significantly lower than in patients with lung cancer.

Abnormalities in the membrane lipid bilayer are caused primarily by lipid peroxidation and endogenous phospholipases [5]. It has been reported that tumor growth is accompanied by activation of lipid peroxidation and a decrease in the content of lipid antioxidants and thiols in various tissues, in particular, in blood erythrocytes [2,6,11].

When analyzing the composition of the erythrocyte membrane lipids, we found an increased content of cholesterol (CH) in patients with lung, stomach, and colon cancer (Table 1), while in patients with neck and head tumors this parameter practically did not differ from normal. There were no significant differences in the membrane CH content between patients with different tumors. The increased CH content attests to high membrane microviscosity and, consequently, impaired deformability and accelerated elimination of erythrocytes from the circulation [4]. The total content of membrane phospholipids and CH esters in tumor patients did not differ from normal. However, the content of triglycerides in patients with lung cancer was lower than in healthy donors and patients with neck and head tumors (Table 1).

Phospholipids are known to play an essential role in the regulation of erythrocyte membrane structure and function [3,8]. The content of lysophasphatidylcholine (lysoPC) in patients with lung cancer, neck and head tumors, and stomach cancer did not differ significantly from that in healthy donors; in patients with colon cancer this parameter did not differ from the normal, but was significantly lower than in patients with neck and head tumors. Moreover, we observed a negative correlation between the contents of lysoPC and PC in erythrocyte membranes in patients with stomach cancer (Table 2). This can be due to activation of endogenous phospholipases and impaired conversion of lysoPC into PC. Accumulation of lysophosphalipids in erythrocyte membranes facilitates transformation of lipid bilayer into monolayer associated with disturbances in Na^+ and K^+ permeability, formation of hydrophilic channels, and enzyme solubilization [7].

In patients with neck and head tumors, the content of phosphatidylserine in the erythrocyte plasma membrane was considerably lower than in healthy donors and in patients with lung, stomach, and colon cancer. The mean contents of phosphatidylinositides, sphingomyelin, phosphatidylethanol-

TABLE 2. Phospholipid Fractions (%) in the Erythrocyte Plasma Membrane of Tumor Patients (*M±m*)

Group	LysoPC	Phosphatidyl-inositides	Sphingomyelin	PC	Phosphatidyl-serine	Phosphatidylethanolanime	Polyglycerolphosphates	Phosphatidic acids
Healthy donors	7.23±0.53	8.06±0.61	10.38±0.72	22.93±1.41	11.92±0.74	20.54±1.38	8.60±0.77	10.35±0.75
Lung cancer	10.55±0.80**	8.85±0.57	10.96±0.62	20.54±0.83	11.18±0.71	20.07±1.03	8.81±0.73	9.04±0.45
Neck and head tumors	11.14±0.96**	8.68±0.44	11.98±0.60	22.03±1.29	8.36±0.79***°	17.65±0.95	9.80±1.22	10.38±0.92
Stomach cancer	9.36±0.66x	8.69±0.74	10.65±0.58	18.82±1.34*	11.72±1.03°°	18.31±1.31	10.50±0.39	11.54±1.40*
Colon cancer	8.44±0.57°	8.43±0.93	11.25±0.45	22.81±1.69***°	12.16±0.96°°	19.63±1.64	8.36±1.25	8.92±0.88

Note. °$p<0.05$ and °°$p<0.02$ compared with neck and head tumors, ***$p<0.05$ compared with stomach cancer.

anime, polyglycerolphosphates, and phosphatidic acids were similar in tumor patients and healthy donors (Table 2).

Thus, tumor growth is accompanied by marked changes in the lipid spectrum of erythrocyte membranes associated with disturbances in the structure and function of erythrocytes and aggravating the patient's condition.

REFERENCES

1. I. G. Akoev and N. N. Motlokh, *Biophysical Analysis of Prepathological and Preleukemic Conditions* [in Russian], Moscow (1984).
2. S. E. Barmina, V. V. Novitskii, and E. D. Gol'dberg, *Vopr. Med., Khimii*, **39**, No. 3, 28-29 (1993).
3. A. A. Boldyrev, *Introduction into Membranology* [in Russian], Moscow (1990).
4. K. E. Bulegenov, and B. S. Balmakhanov, *Izv. Akad. Nauk KazSSR (Ser. Biol.)*, No. 5, 78-82 (1989).
5. Yu. A. Vladimirov, *Pat. Fiziol.*, No. 4, 7-19 (1989).
6. V. E. Goldberg, A. M. Dygai, and V. V. Novitskii, *Lung Cancer and the Blood* [in Russian], Tomsk (1992).
7. G. A. Gribanov, *Vopr. Med. Khimii*, **37**, No. 4, 2-10 (1991).
8. V. I. Krylov, Yu. E. Vel'tishchev, A. D. Petrushina, et al., *Lipid Metabolism in Children* [in Russian], Krasnoyarsk (1985).
9. M. I. Prokhorova and Z. H. Tupikova, *Advanced Workshop in Lipid and Carbohydrate Metabolism* [in Russian], Leningrad (1965).
10. I. P. Tereshchenko and A. P. Kashulina, *Pat. Fiziol.*, No. 3, 10-15 (1995).
11. B. S. Khyshiktuev, N. A. Khyshiktueva, V. N. Ivanov, *et al.*, *Vopr. Onkol.*, **39**, Nos. 7-12, 288-291 (1993).
12. W. T. Bloor, *J. Biol. Chem.*, **170**, 671-674 (1947).
13. J. N. Bragdon, *Ibid.*, **190**, 517-520 (1951).
14. J. Folch, M. Lees, A. G. H. Sloane-Stanley, *Ibid.*, **226**, 497-509 (1957).
15. D. Steinberg, *Cancer*, **39**, No. 5, 296-304 (1989).