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GLYCOCONJUGATE PROFILE IN PLASMA AND ERYTHROCYTES OF GASTRIC CANCER PATIENTS

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Abstract : The present study has examined the glycoconjugate profile in plasma and erythrocyte membranes of 24 adult male gastric cancer patients and an equal number of age and sex-matched controls. Protein-bound hexose, hexosamine and sialic acid were significantly increased in plasma and erythrocytes of gastric cancer patients compared to controls. Elevation of glycoconjugates in circulation is suggested to be a result of increased shedding by the tumor cells or increased synthesis by liver, due to acute phase response.

Key words : gastric cancer, glycoproteins, sialic acid, erythrocyte membrane, plasma

INTRODUCTION

Several properties of malignant cells are expressed at or mediated through the cell surface. Neoplastic transformation is associated with alterations in cell surface glycoconjugates (1). Sialic acid, a terminal component of the carbohydrate chains of glycoconjugates which plays a vital role in cell contact phenomenon, growth control and cellular invasiveness has been demonstrated to be increased at the surface of cancer cells (2).

In several types of malignancies, glycoconjugate profile has been shown to be altered in circulation (3). Evaluation of plasma glycoproteins has been found useful in diagnosis, early detection and staging of a wide variety of neoplasms. The erythrocyte membrane is an excellent model for membrane studies due to its simplicity, easy availability and ease of isolation. Alterations in erythrocyte membrane have been documented in malignant transformation (4, 5).

Adenocarcinoma of the stomach is a major cause of cancer death in developing countries (6). Several cell surface molecules have been closely linked with gastric tumorigenesis and differentiation (7). Previous reports from this laboratory have shown induction of erythrocyte membrane lipid peroxidation and changes in plasma antioxidants in gastric cancer patients (8, 5). However, information on alterations in the cell surface glycoconjugates in patients with

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gastric carcinoma is limited. The present study was therefore undertaken to evaluate the glycoconjugate profile in plasma and erythrocyte membrane in patients with adenocarcinoma of the stomach.

METHODS

Twenty four untreated patients with biopsy proven stage III adenocarcinoma of the stomach from Rajah Muthiah Medical College and Hospital, Annamalai University, were chosen for the study. All the patients were males ranging in age from 50–60 years. An equal number of normal, healthy volunteers of the same age and sex served as controls.

Blood samples were obtained by venous arm puncture in heparinised tubes. Plasma was separated by centrifugation at 1000xg for 15 minutes. The erythrocyte membrane was prepared as described by Quist (9). Glycoproteins were estimated by the method of Niebes (10) (protein-bound hexose), Wagner (11) (protein-bound hexosamine), Warren (12) (total sialic acid) and Katapodis and Stock (13) (lipid-bound sialic acid, LSA). Statistical analysis was done by Student's 't'-test.

RESULTS

Table I shows the glycoconjugate levels in the plasma and erythrocyte membrane of gastric cancer patients and normal subjects. Plasma protein-bound hexose, protein-bound hexosamine, total sialic acid and lipid bound sialic acid were significantly increased in gastric cancer patients as compared to normal. The levels of protein-bound hexose, protein-bound hexosamine and total sialic acid in erythrocyte membrane were also increased in gastric cancer patients compared to normal subjects.

TABLE I : Glycoconjugate profile in plasma and erythrocyte membrane of control and gastric cancer patients.

Parameters	*Control*	*Gastric cancer*
Plasma		
Protein-bound hexose	104.3 ± 22.4	179.8 ± 48.6**
Protein-bound hexosamine	74.4 ± 11.8	108.2 ± 19.6**
Total sialic acid	65.3 ± 7.3	109.2 ± 9.6**
Lipid-bound sialic acid	17.6 ± 2.3	23.6 ± 3.4**
Erythrocyte membrane		
Protein-bound hexose	130.4 ± 17.5	145.2 ± 19.4*
Protein-bound hexosamine	93.4 ± 18.1	109.1 ± 7.5**
Total sialic acid	45.3 ± 6.8	63.8 ± 9.8**

Data represent mean ± SD from 24 subjects in each group.
Values are expressed as mg/dl for plasma and μg/mg protein for erythrocyte membrane.
*P<0.01; **P<0.001.

DISCUSSION

Several studies have shown a positive association of glycoproteins with malignancies. Lipton et al (3) have reported a significant increase in the levels of plasma glycoproteins in patients with a wide variety of neoplasms. In endoscopic gastric biopsies from stomach cancer patients, hexose content was found to be increased, whereas N-acetylgalactosamine was significantly decreased (14). Extremely high concentrations of hexosamine were found in the gastric mucus of patients with gastric adenocarcinoma (15). The increase in the levels of glycoproteins in the plasma and erythrocyte membrane of gastric cancer patients observed in the present study may be a reflection of changes at the tumor cell surface.

Evaluation of plasma sialic acid as a reliable tumor marker has been well documented (16). A marked increase in plasma total and lipid-bound sialic acid has been reported in colon cancer (17). Elevation of plasma sialic acid has been observed in patients with lymphoma, malignant melanoma and cancers of the prostate, bladder and gynecologic system (18, 19). Measurement of LSA along with other clinical and biochemical criteria has been suggested to be valuable in diagnosis, staging, detecting metastasis and evaluating therapeutic response. Katopodis and Stock (13) have reported that LSA may be a more useful marker than total sialic acid.

Mammalian tissues are composed of neutral glycoproteins with the same carbohydrate constituents as that of plasma supporting the possibility of increased local production and direct release into circulation (20). A prominent component of the host response to a malignant tumor is the synthesis of a set of glycoproteins by the liver and subsequent release into circulation (21). Kloppel et al (22) have suggested that neoplasms often have an increased concentration of sialic acid on tumor cell surface, and sialoglycoproteins are shed or secreted by neoplastic cells increasing the levels in blood. Hence, the enhanced levels of plasma glycoproteins in gastric cancer patients may be due to increased hepatic synthesis or increased shedding from the tumor into circulation.

Thus, the present findings indicate profound alterations in the glycoprotein profile of patients with adenocarcinoma of the stomach. Efforts are underway to correlate elevated levels of glycoproteins in circulation with alterations at the tumor cell surface.

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