ONCOLOGY

Changes in the Content of Protein and Lipid Oxidative Modification Products in Tumor Tissue at Different Stages of Lung Cancer

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 147, No. 5, pp. 562-563, May, 2009
Original article submitted March 5, 2008

The content of LPO products (conjugated dienes, MDA) and products of oxidative modification of proteins (protein carbonyl derivatives) is reduced in tumor tissue in comparison with normal tissue and varies depending on the disease stage.

Key Words: *oxidative modification of proteins; lipid peroxidation; lung cancer*

Malignant tumors of the lungs are among the most prevalent oncological diseases. Chronic inflammation and exposure to atmospheric pollutants make an appreciable contribution to carcinogenesis and development of precancer states [4,11]. They stimulate free-radical oxidation in cells, which are regarded as a universal mechanism of tumor transformation [4]. The appearance and development of tumor are associated with changes in the antioxidant system and free-radical oxidation, but the intensity and direction of these changes are insufficiently studied [4]. Free-radical oxidation processes in tumor cells are interesting objects of study, because they determine such processes as angiogenesis and apoptosis, cell recognition by leukocytes, *etc.* [1,2,5,7]. We evaluated the intensity of free-radical oxidation in normal and tumor tissues of patients with lung cancer at different stages of the disease.

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MATERIALS AND METHODS

A total of 87 patients (male) with lung cancer aged 30-55 years were examined at Krasnoyarsk Territorial Oncological Center. Specimens of tumor and normal lung tissue were collected during surgery. The levels of protein oxidative modification products (carbonyl derivatives) and LPO products (conjugated dienes (CD) and MDA) were measured in tissue homogenates.

The level of protein carbonyl derivatives (PCD) was evaluated by the reaction of oxidized amino acid residues of proteins with 2,4-dinitrophenylhydrasine with the formation of 2,4-dinitrophenylhydrasones, detected by spectrophotometry at λ=370 nm [10]. The content of CD was evaluated by absorption intensity at λ=232 in heptane extract of tissue lipids [3]. The content of MDA was evaluated by the reaction with TBA resulting in the formation of a colored complex with the absorption maximum at λ=532 nm [6].

RESULTS

Lipids and proteins are important cell targets of free-radical activity. LPO markers detected most

0007-4888/09/1475-0630

TABLE 1. Content of Oxidative Stress Markers in Tissues at Different Stages of Lung Cancer (*M*±*m*)

Stage	PCD, μmol/mg protein	CD, μmol/mg protein	MDA, μmol/mg protein
Control (*n*=73)	23.06±0.85	3.826±0.042	3.317±0.029
Stage I (*n*=9)	—	1.822±0.074*	2.229±0.121*
Stage II (*n*=26)	11.66±0.60*	1.964±0.029*	2.227±0.095*
Stage III (*n*=35)	17.60±0.81*	2.893±0.078*	3.381±0.129*
Stage IV (*n*=17)	12.18±0.68*	2.515±0.073*	2.823±0.071*

Note. *$p<0.05$ compared to the control.

frequently are CD and MDA. Oxidative modification of proteins can be realized by direct oxidation of amino acid residues, by reaction with LPO products (MDA, 4-hydroxy-2-nonenal), and glycoxidation. All these mechanisms introduce carbonyl groups into protein molecules and can lead to irreversible loss of their biological activity. Hence, carbonyl derivatives of proteins can serve as markers of general oxidative stress. In addition, PCD are stable compounds and hence, are preferable in comparison with lipid peroxides as indicators of oxidative stress.

The content of LPO products and products of oxidative modification of proteins is reduced significantly in the tumor in comparison with normal tissue (Fig. 1). Presumably, the intensity of oxidative processes decreases as a result of activation of antioxidant enzymes [1,8,9] or of decreased production of active oxygen forms [4]. Since reactive oxygen forms play a certain role in the development of apoptosis [2,5], the decrease in their content can be a mechanism protecting cancer cells from apoptosis. In addition, low intensity of LPO can impair macrophage and neutrophil capacity to recognize tumor cells [1,2,8].

The content of PCD, CD, and MDA in the tumor depends on the stage of the disease (Table 1). It is minimum at stage I and reaches the peak at stage III, after which (stage IV) these values somewhat decrease. Hence, we can speak about phenotypical changes in the tumor over the course of tumor progress. These data are in line with the results indicating high antioxidant potential of tumor cells making them more resistant to various factors.

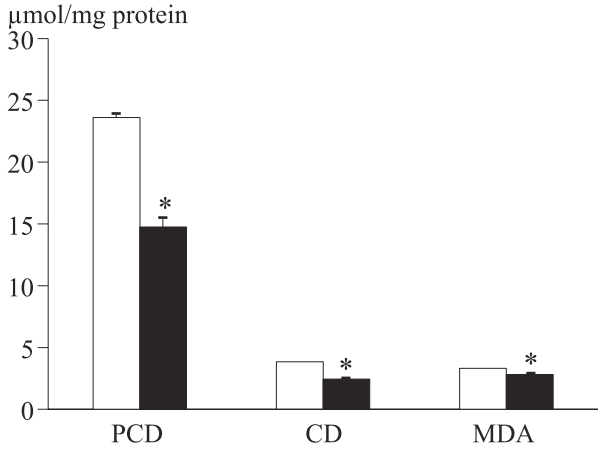

Fig. 1. Content of oxidative stress markers in lung tissue. Light bars: control; dark bars: patients with different stages of cancer. *$p<0.05$ compared to the control.

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