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Radioiodine therapy accelerates apoptosis in peripheral blood lymphocytes of patients with differentiated thyroid cancer

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Both apoptosis and micronuclei formation reflect cytogenetic damage in cells and could contribute to cell homeostasis. The aim of this study was to evaluate apoptosis in peripheral blood lymphocytes (PBLs) of patients with differentiated thyroid cancer (DTC) before and after 131-iodine (131-I)-therapy and its correlation with micronuclei (MN) frequency. The study population included 18 DTC patients and 18 healthy donors. Apoptotic cells were detected using the Annexin V-FITC/7-AAD kit and MN frequency by cytokinesis-block MN assay. The difference between early apoptosis in PBLs of DTC patients before therapy and controls (9.88 ± 4.99% vs. 6.64 ± 2.07%, p = 0.003) was significant, as well as between early apoptosis in PBLs of DTC patients before and after 131-I-therapy (9.88 ± 4.99% vs. 13.53 ± 6.57%, p = 0.008). The MN frequency and early apoptosis in PBLs of DTC patients was positively correlated before (r = 0.540, p = 0.021) and after 131-I-therapy (r = 0.585, p = 0.014). Thyroid cancer patients had a significantly increased early apoptosis in PBLs, which further increased after 131-I-therapy in association with MN frequency.

Key words: apoptosis, differentiated thyroid cancer, micronuclei, peripheral blood lymphocytes, radioactive iodine

Apoptosis is a physiological process involving many morphological and biochemical changes whereby most cells are eliminated. The typical morphological changes are shrinkage of the cell, fragmentation into membrane-bound apoptotic bodies and rapid phagocytosis by neighboring cells [1, 2]. During the process of apoptosis, the appearance of phosphatidylserine on the outer leaflet of the cell membrane occurs relatively early in cells in which the integrity of the cell membrane is maintained and facilitates non-inflammatory phagocytic recognition of apoptotic cells [3, 4]. In the late stage of apoptosis, the integrity of the cell membrane is lost [4, 5].

Deregulation of apoptosis may be of primary importance in the pathogenesis of many diseases [6]. Spontaneous *ex vivo* apoptosis of circulating peripheral blood lymphocytes (PBLs) has been evaluated in patients with head and neck carcinoma [7], carcinoma of the digestive tract [8] and reproductive system [9, 10], breast carcinoma [11], melanoma [12] and multiple myeloma [13]. Therapy applied to patients with different types of tumors may accelerate apoptosis of malignant cells, so increase in apoptosis might be a suitable target for therapy [14, 15, 16].

Micronuclei (MN) are chromosomal fragments or whole chromosomes that are not included in the nuclei during division. They appear in the cytoplasm of daughter cells as small additional nuclei [17]. PBLs of cancer patients have a higher micronuclei (MN) frequency than those of healthy persons [18, 19, 20], which additionally increased after therapy [21, 22]. Both apoptosis and micronuclei formation reflect cytogenetic damage in cells and could contribute to cell homeostasis.

The MN frequency in PBLs of patients with differentiated thyroid cancers (DTCs) before and after 131-I therapy has already been studied [23, 24, 25], but the level of apoptosis in PBLs of patients with DTC treated with 131-I has not been investigated so far. The aim of our study was to determine the level of apoptosis of PBLs in thyroid cancer patients before and after 131-I therapy, and to correlate its intensity with MN frequency.

Patients and methods

Study population. The study was approved by the Ethical Committee of the Clinical Center Kragujevac. All patients and