AUTOIMMUNE RESPONSE IN LUNG CANCER PATIENTS WITH NEUROLOGICAL PARANEOPLASTIC SYNDROMES

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Background: The cellular immune response is activated as a part of antitumor reaction of the malignancy-bearing host. Neurological paraneoplastic syndromes (NPS) are defined as indirect effects of cancer on the nervous system and considered to be immune-mediated. The stimulation of immune system in such cases may limit the aggressiveness of cancer, development of metastasis, and improve the survival. Granzyme B and perforin pathway, as well as Fas ligand-Fas receptor interaction play important role in cytotoxic response. The aim of the study was to evaluate granzyme B, perforin and Fas ligand (FasL) expression in peripheral blood mononuclear cells (PBMC) in lung cancer patients considering NPS. **Methods:** We included in the study 52 patients with NPS (28 cases) hospitalized in the Clinic of Neurology at Poznan University of Medical Sciences and with diagnosed lung cancer (24 cases) admitted to Department of *Pulmonology,* Allergology and Respiratory Oncology, Poznan University of Medical Sciences. The NPS were diagnosed basing on Graus criteria. The presence of well-defined onconeural antibodies (anti-Hu, anti-Ri, anti-Yo, anti-Ma/Ta, anti-CV2, anti-amfiphysin) was detected by means of indirect immuoflurescence and if positive - confirmed with Line Blotting (Euroimmun). Indirect immunofluorescence enabled also the detection of other antibodies (anti-myelin, anti-neuroendothelium, anti-MAG, anti-GAD). PBMC were isolated from heparinized blood samples by concentration gradient centrifugation (Ficoll Paque Plus, Healthcare) and freezed in -70ºC until analysis. PMBC lysis was carried on with the use of lysis buffer containing the coctail of proteinase inhibitors. In the next step the expression of granzyme B (Abcam), perforin (Abcam), FasL (Enzo Life Sciences) was detected in supernatant by means of ELISA. The protein concentration was estimated by means of Lowry method. **Results:** The study group consisted finally of 30 (58%) lung cancer patients, 9 (17%) ovarian cancer, 2 (4%) prostate cancer, 2 (4%) with other malignancies and 9 (17%) cases without identified malignancy. Clinically 20 (64,5%) patients manifested peripheral (polyneuropathy/neuropathy, myasthenic syndrome, myopathy) and 11 (35,5%) - central syndromes (cerebellar syndrome, motor neuron disease, extrapyramidal syndrome). In 15 (29%) patients the presence of well-defined onconeural antibodies was detected and in 34 cases (65%) other autoantibodies were found. In lung cancer patients 8 (27%) had well-defined onconeural antibodies and 8 (27%) – other autoantibodies. The expression of FasL in PBMC (7.39; 0.02-11.87 pg/mg of protein; median; interquartile range) was increased (P=0.0171) comparing to other groups of patients (0.027; 0.01-5.73 pg/mg of protein). The Granzyme to FasL ratio differed (P=0.0180) between lung cancer patients with peripheral (11589; 166-58242) and central NPS (73; 34-112). In multiple regression analysis in the model including sex, the presence of small cell lung cancer, onconeural antibodies and NPS, sex was an independent factor influencing the PBMC expression of Granzyme (B=1536; P=0.0126) and perforin (B=30925; P=0.0174). **Conclusions:** FasL expression in PBMC is up-regulated in lung cancer patients. The interplay between granzyme B and FasL may be involved differently in the development of NPS at the level of peripheral and central nervous system in different manners. Gender has influence PBMC expression of granzyme B and perforin in lung cancer patients.