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IMMUNOLOGICAL STATUS OF DIFFERENT CATEGORIES OF POPULATION AFTER CHERNOBYL ACCIDENT

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Abstract

Investigation of immune status of the victims of the Chernobyl Nuclear Power Plant (NPP) accident irradiated in diferent doses was performed. Acute postradiation immunodefficiency in heavily exposed persons was changed in 6 - 24 months to the 5-7 year period of restitution and the latter was succeded by normalisation of CD3+, CD4+, CD11+ cell count and serum IgG and IgA content in certain patients, while the others revealed immunologic defficiency of the mixed type. HLA-antigenic combinations connected to the increased radiosensitivity were found out. Elaboration of in vitro tests for surface antigens expression in response to thymic peptides allowed to make adequate immunocorrection if needed.

Immune system plays a crucial role both at the early stage of radiation injury and in the realisation ot remote effects of irradiation. Immunological follow-up of different kind of victims of the Chernobyl (NPP) accident are of interest for drowing conclusions about actual health conditions and prediction of the development of different somatic diseases and functional disorders [1].

The investigations in the Department of Clinical Immunology of the Research Centre for Radiation Medicine of the Academy of Medical Sciences of Ukraine since its creation in 1987 were directed to the field of the possible mechanisms of radiation effects and the evaluation of the role of random alteration of common bone marrow progenitor cells by quants of radiation and non-lethal damage of regulatory systems, especially in the case of small absorbed doses of acute or continious partial irradiation. Immunological investigations included flow cytometry quantification of cell subpopulations, HLA-typing and humoral immunity study as previously described [2].

Person with different absorbed doses (from 0.05 Gy to the doses inducing acute radiation sickness - 1 -3 Gy) were taken into account .

A process of the three stage of the immune system recovery was seen in persons who suffered from acute external irradiation. Dynamic investigations of immune state revealed a postradiation defficiency. The cellular or/and humoral immunity disturbances included surface phenotype changes, especially in mitogen-associated subpopulations of CD3+, CD4+ and NK- cells (CD57+, CD11+16+). It was worth to mention the mozaic of injury and reparation of surface membranes of immunocompetent cells. B-cells exhibited the short-time decrease of C3+ and pan-B-antigen bearing cells subpopulations. Membrane changes at that time also evoked the difficulties in locus A, B, C HLA-typing. . First stage lasted from 6 to 24 months, the absorbed doses and the duration of irradiation, the presence of somatic and psychosomatic pathology, age at the moment of irradiation influenced greatly on this stage lasting .

The second stage was characterized by the restitution of the radiation injury, the increase of subpopulation of CD3+DR+ lymphocytes was seen , accompanied by stable

tendencies of finding in the peripheral blood of lymphocytes bearing CD4+8+ and CD1+ antigens, which normally were characteristic only for intrathymic stages of T-cell differentiation. There were the increases of B-lymphocytes count, which had such pan-B-markers as CD21, C3, late differentiation markers such as surface IgG and early antigens as CD10. These findings without leukemic reactions suggested about existence of some constrains in the immune system function and their possible role of the background of future immunopathologic processes. The decrease in expression of some antigens normally presented on monocyte cells was revealed by performed study. HLA-Dr-antigens coexpressed with LeuM3 with high fluorescence intensity (560.0+1.0) were seen only on 3.0+0.1% of cells. There were not any coincidence between CD57+ and CD11+16+ cell counts, the latter subpopulation was determined as highly active natural killers.

A study of T-cell receptor stable alterations was performed among the population of contaminated territories inhabitants and personnel of the Chernobyl NPP. A two-fold increase of aberrant cells (0.4- 0.6 per cent of the peripheral mononuclear cell) with decreased TCR expression was found in investigated contingents in 1990 - 1992.. It was accompanied by the 2 -3 fold increase of glycophorin A (GPA) aberrant red blood cells. Next years the quantity of aberrant T-cells slovly diminished, GPA mutant cells remained constant.

Major hystocompatibility typing revealed in locus I the prevalence of HLA-A1, 28; HLA-B5, 38; HLA-B16, 17; HLA-B17,18; HLA-B8, 22; HLA-B 8, 27; HLA-B 27, 35; HLA-A1, B16; HLA-A1, B27; HLA-A2, B38; HLA-A10, B38; HLA-A28, B8 in patients, who had suffered from acute radiation sickness comparing to the group of Chernobyl clean-up workers with the absorbed doses reaching or exceeding 1 Gy, but without acute radiation injury of bone marrow. These data are very important for the estimation of the radiosensitivity in individuals exposed to the lower doses and for NPP workers professional selection.

To our mind, any genetic research results could be valuable only in connection with characteristics of the given geno-geographic zone. For example, we foun out that HLA-A1,9; HLA-B8,12; HLA-B12,13; HLA-B15,35 antigen combinations were associated with thyroid pathology both in contaminated and non-contaminated regions of Ukraine with no differencies depended on radiation influence.

As a third stage of immune system recovery in five-seven years after the irradiation a heterogeneity of types of immunologic response of acute radiation sickness reconvalescents was detected. A group of patients demonstrated normalisation of CD3+, CD4+, CD11+ cell count and serum IgG and IgA content, while the others revealed immunologic defficiency of the mixed type.

Subset cell cycle analysis with propidium iodide showed the decreased prolipherative response to concanavalin A (Con A) in 18 hour cultures as well as 3H thymidine uptake in 72 hours cultures. Dose-dependent changes of enkephaline receptor on peripheric blood mononuclear cells (PMNC) and sensitisation to brain antigens accompanied by changes of TrR, RIL-2, CD10, CD23 activation antigens expression were seen in healthy irradiated persons as well. Late radiation and functional effects could be explained by neuro-humoral regulatory changes.

Clinical and immunologic investigation was performed in the group of Chernobyl clean-up workers and the personnell of nuclear power plant suffering from vegetative dysfunctions. Correlative dependencies were shown between Leu4+HLADR- cell count, on one hand, and the time of working in the zone of elevated irradiation (r=-0,72), on the other hand, Leu3a+2a+ (r=0,64), Leu3a+2a- (r=-0,68) and the absorbed doses. CD4+ cell decrease was predominantly due to Leu3a+8- inductors of antibody producing cell decrease. Subset cell cycle analysis (SOBR) showed increase of heterogenity, non-replicative DNA synthesis in short term culturewith Con A, cortisol, 5-hydroxytryptamine and epinephrine in patients with vegetative dysfunctions irradiated in low doses interval.

The presence of combined changes in immune status of various population groups irradiated in Chernobyl accident caused the difficulties in the solving the problem of individual immunocorrection necessity.

We elaborated an in vitro sensitivity assays for CD3, CD10, HLA-Dr expression in response to thymic peptides and performed them in 1120 patients. It was shown that irradiated individuals had exhibited different types of response to thymic derivatives with the dependence on absorbed doses, initial state of immunologic reactivity and the character of somatic diseases. A distinct increase of antigen expression was revealed in leukemia patients. In vitro results showed good correlation with the clinical effectiveness of above mentioned immunomodulative thymic peptides.

Comprehencive clinical and immunologic investigation of persons in various exposed groups led to the conclusion that the control of cell differentiation should be the key point in late immunological effects of irradiation. Exact mechanisms of these pathways will be a subject of future investigations.

References

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