RADIATION&APPLICATIONS
ISSN 2466-4294 (online) | rad-journal.org
Vol. 2 | Issue 1 | pp. 5 – 9
doi: 10.21175/RadJ.2017.01.002
Original research paper

IMMUNE SYSTEM ASSESSMENT OF THE CHERNOBYL NUCLEAR POWER PLANT DISASTER CONSEQUENCE LIQUIDATORS*

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Abstract. *The observation of the liquidators of the Chernobyl accident has shown that as time goes on, they have different pathological processes and chronic illnesses. Increased level of chromosome aberrations, immune and endocrine disorders, clastogene factors etc., requires active treatment and rehabilitation measures. We have studied the changes in the immune system of the liquidators in combination with the other vital systems of the organism activity and not in isolation. The condition of cell-mediated immunity was assessed based on the relative and absolute quantity of T- and B lymphocytes. The assessment of the humoral immunity condition was carried out by the estimation of Ig G, Ig A, Ig M class immunoglobulin concentration in the serum. Non-specific defense factors are the complement content in the serum and phagocytic activity of the neutrophils. Statistical analysis of the data was carried out with the help of such methods of system analysis as correlation, variance factor and cluster analysis. Making use of the method of the assessment of human immune system suggested by L.V. Kovalchuk and A. N. Cheredeev, based on the pathogenetic principle, we developed an algorithm of assessment of humoral component of immune system in case of immunodeficiency. In spite of the seemingly good condition of the immune system in the early post-accident period, which can be accounted for by adaptation mechanisms, in most cases (63.8%), a recurrence of inflammatory processes is observed, which is probably explained by the displacement of the immune system component provoked by radiation influence 20-25 years ago, with non-radiative factors connected with the way of life.*

Key words: *Immunological disorders, liquidators, radiation and age factors, algorithms, humoral immunity, cell-mediated immunity*

1. INTRODUCTION

In spite of the 30-year period following the global radio-ecological catastrophe on the Chernobyl nuclear power plant, the issues of examination, treatment and rehabilitation of victims are still up to date. Over 2500 liquidators of Chernobyl nuclear power plant catastrophe have been under observation at the Centre of Radiation Medicine and Burns for over 30 years.

The observation of the liquidators of the Chernobyl accident has shown that as time goes on, they have different pathological processes and chronic illnesses. And at the same time it is characteristic of functional changes to gradually become organic diseases of cardiovascular system, respiratory organs, nervous system, locomotor apparatus. Increased level of chromosome aberrations, immune and endocrine disorders, clastogene factors etc., requires active treatment and rehabilitation measures.

At present clinical immunology is the link between a great many of medical disciplines. Its main objectives include diagnostics, prognosis and development of treatment methods of diseases accompanied by various immune system disorders.

It is common knowledge that immune system is directly involved in the pathogenesis of both early and ultimate consequences of radiation damage. The authors [1] have noted that changes in the immune system should be studied in combination with the other vital systems of the organism activity and not in isolation. A comprehensive assessment of the condition of immune system components has to take into account both qualitative and quantitative indicators of immunity. Taking into consideration the above mentioned, we have made an attempt to assess the immunological indicators in complex.

2. MATERIALS AND METHODS

246 liquidators of the Chernobyl nuclear power plant catastrophe have been examined continuously. The control group was comprised of 84 practically healthy people aged 30-50. In addition to the routine peripheral blood test (hemoglobin, erythrocytes,

* The paper was presented at the Fourth International Conference on Radiation and Applications in Various Fields of Research (RAD 2016), Niš, Serbia, 2016.

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globular value, reticulocytes, platelets, leukocytes, myelocytes, metamyelocytes stabs, segmentated cells, eosinophils, basocytes, lymphocytes, monocyte and the speed of erythrocyte sedimentation) relative and absolute quantity of T-lymphocytes and rosette-forming cells (naked cells), serum immunoglobulin (IgG, IgA, IgM), phagocytic and complementary activity were studied.

The immunological examination in the Scientific Centre of Radiation Medicine and Burns was based on a combination of methods, approved by the methodological recommendations "Assessment of the human immune status" [2].

The condition of cell-mediated immunity was assessed based on the relative and absolute quantity of T- and B lymphocytes. The assessment of the humoral immunity condition was carried out by the estimation of Ig G, Ig A, Ig M class immunoglobulin concentration in the serum. Non specific defense factors are the complement content in the serum and phagocytic activity of the neutrophils.

For immunological tests lymphocytes were separated from venous blood in the ficoll-verografin gradient. T- lymphocytes were identified with the method of spontaneous resetting with sheep erythrocytes, B- lymphocytes- with mice erythrocytes, the level of serum Ig G, Ig A, Ig M immunoglobulins – with the method of radial displacement by Manchiny; complementary activity by 100% haemolysis; phagocytic activity of the neutrophils in relation with the staphylococcus.

All the liquidators under examination were divided into 3 groups in accordance with the year of their stay in the disaster area (1986, 1987 and 1988).

On the assumption that the standards of some immunological indices vary with the age [3,4,5], an attempt was made to study the immunological status of the examined liquidators by dividing each of the above mentioned groups into 3 age subgroups (1930-1940;1941-1950;1951-1960).

In addition to age the indices of immunity and non specific reactivity of the organism depend on seasonality, gender, natural and climatic factors, temperature impact, environmental adaptation, professional factors and the way of life. But of all the factors listed above age can be better interpreted.

Statistical analysis of the data was carried out with the help of system analysis methods (correlation, variance factor and cluster) [6]. The analysis of the material was worked out with the help of well-known computer programs intended for statistical processing of data array as well as with programs worked out by us. The Microsoft Excel spreadsheet and special-purpose statistical packages StatSoft and StatGraphics Plus [7,8] were made use of.

3. Results and Discussion

The examination results right after return from the disaster area show that there were no statistically significant changes in the number of leukocytes, lymphocytes, relative and absolute number of T- and B- lymphocytes in all age groups. There were no significant fluctuations in serum immunoglobulins and in complementary and phagocytic activity of neutrophils. An abrupt increase in the size of lymphocytes was observed in some patients.

A significant increase of leukocytes is observed from 1987. It was (9.5±0.7)x10^9/l compared to the control group (6.9±0.3)x10^9/l in case of liquidators. It can be seen in Figure 1(b) which describes the part of influence of age and radiation factors on the quantity of leukocytes, that in the first years following the Chernobyl catastrophe up to 1991 the share of radiation factor prevails over that of age and probably significant increase in leukocyte level is mainly attributed to radiation factor influence. Starting from 1991 essential changes in the cells of the white germ are not discovered.

Leukocyte cell rejuvenation was noticed in the early post disaster period, the evidence being the increase in stab (2.2±0.2 compared to control group: 0.4±0.1) and segmented neutrophil (65.6±1.7 compared to control group 58.3±1.5) and eosinophil content (1.6±0.1, in control group 3.0±0.7). 68-72% of patients showed decrease in lymphocyte (28.9±1.3 compared to control group 33.4±1.2) and monocyte (3.03±0.3, in control group 4.8±0.5) content. The observed deviations are obviously the result of the disorder of balanced condition and are a consequence of proliferation disorder and marrow cell maturation.

The relative increase in the leukocyte level in the long-term period (starting from 2002) is obviously connected with weakening of defense reserves due to age and other factors of nonradiative character.

In the first years following the disaster lymphocytosis was also observed which was apparent with the liquidators who took part in the work of the emergency team in 1986. Factor analysis demonstrated that lymphocyte number decrease was mainly due to radiation factor (Fig. 2), which by the end of the study was at an insignificant level. Starting from 2002, age factor influence reached a significant level.

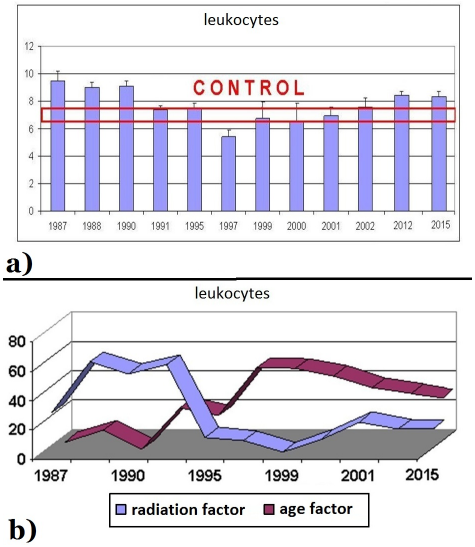

Figure 1. The dynamics of the change in the leukocyte level (a) and the results of the variance factor analysis (parts of influence of the radiation and age factors (b))

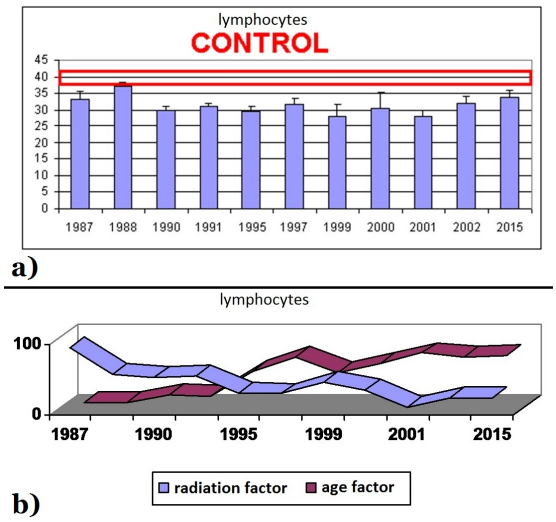

Figure 2. The dynamics of the change in the lymphocytes level (a) and the parts of influence of the radiation and age factors (b)

During the examination of the cell component of the immune system deficiency of the relative number of T-lymphocytes was detected (Fig. 3) against the background of the decrease of their absolute number connected with leukocytosis in the first years of the examination. Variance factor analysis also revealed increase of radiation factor influence which conforms to the data by I. E. Gurmanchuk [9], G. D. Kharitonik [10] and other authors. It is common knowledge that the decrease in the number of **T-** lymphocytes and functional activity can be a decisive factor in the development of consecutive infection and long-term effects after radiation [11].

In the course of the study of the number of B- lymphocytes decrease in their percentage in blood in the first years following the disaster (Fig. 4).

During the following years (1990, 1991) this index was normalized which then changed to recurring descent. As for the radiation factor it was significant in the early period. By 1990 the influence of both radiation and age factors on this index is insignificant and they remain so till the end of the research. Apparently there are more essential factors influencing the change in the number of B- lymphocytes.

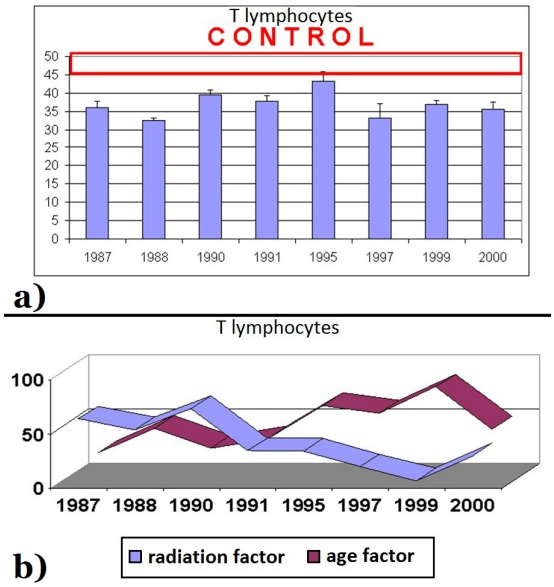

Figure 3. The dynamics of the change in the relative number of T-lymphocytes (a) and the results of the variance factor analysis (parts of influence of the radiation and age factors (b))

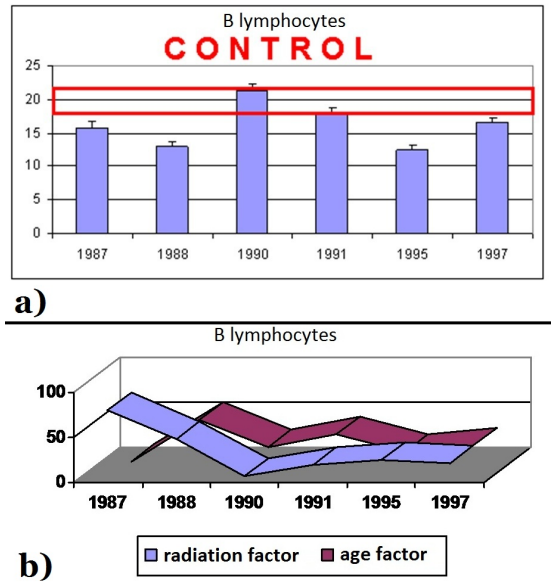

Figure 4. The dynamics of the change in the relative number of B-lymphocytes (a) and the results of the variance factor analysis (parts of influence of the radiation and age factors (b))

While studying the dynamics of the change in the number of immunoglobulins M we noticed a clear tendency of increase in the course of the examination period (Fig. 5a). The influence of the radiation factor on this index can also be noted in the early period after the disaster (Fig. 5b). But later on the radiation factor gives way to the age factor and by the end of the research the influence of the radiation factor is 3.09%.

As the complex estimation of IgA, IgM, IgG immunoglobulin content plays a vital role in the differential diagnostics of various diseases, we also studied the dynamics of the change of IgA and IgG and carried out correlation analysis between these indicators.

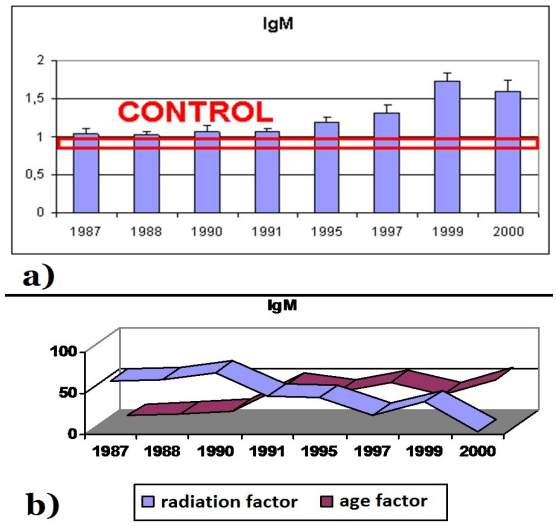

Figure 5. The dynamics of the change in the quantity of IgM (a) and the results of the variance factor analysis (parts of influence of the radiation and age factors (b))

Significant correlation coefficients are discovered: IgA and IgM (r=0.57); IgG and IgM (r=0.66) in the early period; IgA and IgG (r=0.52); IgA and IgM (r=0.57) in the distant period.

Interesting data were obtained in the study of non specific defense factors. In particular, the level of complement in the blood serum decreased in the first year of stay in the disaster area in the 63% of the examined patients in 1986 (Fig. 6), in 59% in 1987, in 20% in 1988 which implies dose dependence and which was proved by factor analysis for that index (maximum value of the influence rate on the complement titer was registered in 1987 and was 81.42%).

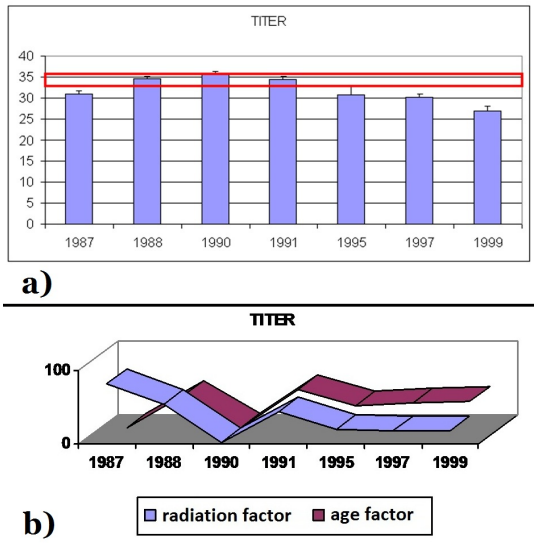

Figure 6. The dynamics of the change of the level of complement (a) and the results of the variance factor analysis (parts of influence of the radiation and age factors (b)).

Inhibition of functional activity of peripheral blood neutrophils is worth mentioning which shows itself mostly by the decrease in the phagocytic number. Meanwhile, the decrease of absorbing capacity of peripheral blood neutrophils is one of the factors contributing to the development of infectious complications.

4. Conclusion

Thus, the examination results of the liquidators right after return from the disaster area show that there were no statistically significant changes in the number of leukocytes, relative and absolute number of **T- and B-** lymphocytes in all groups. There were no significant fluctuations in serum immunoglobulins and in complementary and phagocytic activity of neutrophils. An abrupt increase in the size of lymphocytes was observed in some patients.

Immunodeficiency symptoms emerged only 6 months or a year later. In 1987, cell immunodeficiency was detected, which showed itself with the decrease in the T-dependent immunity component increase in the B-lymphocytes, dissonance between T- and B-lymphocytes with the increase in M immunoglobulins, inhibition of neurtrophil immunophagocytosis.

Making use of the factor analysis we managed to detect the influence of radiation and age factors on the change of immune indices. In this article we studied the influence of the 2 above mentioned factors. Meanwhile, it is well known that in addition to the radiation influence, a number of non radiation factors influencing both in the period of the disaster liquidation (living conditions of the zone, routine change, tense physical and mental work, stress etc.) and in the post disaster period (additional stressful conditions: earthquakes, way of life etc.) should be taken into consideration.

Apparently, the detected changes of the immune status are stipulated by the impact of all these factors in combination.

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