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AUTOIMMUNE PROCESS IN CNS UNDER Cs-137 INNER IRRADIATION

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INTRODUCTION

Autoimmune hypothesis as to the development of radiation-induced brain injuries stands high among the concepts of the CNS post-radiation damage pathogenesis.

To study the changes occurring in a living organism affected by a small-dose radiation due to incorporated radionuclides as well as to create adequate models are of critical importance in the post- Chernobyl period.

The effects of chronic small-dose inner radiation on the development of autoimmune responses were evaluated by determining the level of the CNS proteins and protein-induced antibodies to the CNS components.

MATERIALS AND METHODS

Forty eight ordinary mice weighing 140-180 g were used throughout the experiments. The mice were kept on isocaloric diet in vivarium and received 600 Bk of Cs-137 with food daily. The control group mice (n=16) were kept under similar conditions out of isotopic unit being given similar food free of Cs-137.

The tests were performed after 1,3,6,9 months since the beginning of experiments and in 3 months after a 6-month Cs-137 intake has been terminated.

After 1,3,6,9 months the animals were decapitated, and the blood were taken for serum. In the serum of experimental mice we studied the content of autoantibodies to neurospecific proteins (NSP): MBP, S-100 and NSE (neurospecific enolase) as well as the availability of blood-circulating MBP and NSE. NSP were obtained from calf brain. MBP was isolated using Palladin et al.(1970) technique while S-100 and NSE were isolated after G.A.Berezhnoy (1978). Antibodies to NSP were determinated by the Voller et al (1979) method modified by T.M. Cherenko (1989) using indirect immunoferment technique. To determine the MBP content in the blood serum standard ELISA modified by T.M.Cherenko was used. NSE serum concentration was measured using a set of reagents for NSE assay in human blood serum (NSE EIA <DIAplus>, F.Hoffman-La Rosch & Co., Basel, Switzerland).

RESULTS AND DISCUSSION

Analysis of mean levels of antibodies to MBP shows that at the initial stage of inner ionizing radiation their concentration holds low. However, starting from 3-6 and 9 month particularly, it increases definitely. Titres of autoantibodies to S-100 and NSE were seen to grow gradually within 1-9 months.

In mice with a 3-month interval after a 6-month radiation exposure mean levels of antibodies to all the three NSP have reached control values. The level of autoantibodies to MBP in these mice slightly exceeded the control values, whereas levels of autoantibodies to S-100 and NSE were indefinitely lower.

The most statistically confident autoantibody accumulation against standard value was observed within 6 months (to S-100) and 9 months (to MBP and NSE).

While studying the development of neurosensitization it appeared that autoantibodies to the three NSP: glia markers, neurons and myelin were identified not in every mouse. Out of the mice

having a 1 - month Cs-137 intake only 30 % revealed autoantibodies to NSE and S-100. In this period autoantibodies to myelin structures are not yet registered.

After 3 months of radiation exposure autoantibodies to MBP are also revealed in 80 % of animals. In 9 months autoantibodies to all the three NSP are identified. Practically half of the animals under test exhibit autoantibodies to MBP and NSE while autoantibodies to S-100 appear less frequently.

Thus, it may be concluded that: 1) Not all the animals develop autoimmune responses; 2) Autoantibodies to different antigens are revealed with different frequency. Throughout all experimental periods autoantibodies appear mostly to glia and neuron proteins, whereas autoantibodies to MBP are seen in more prolonged time (from the 3-rd month), being found, however, in the majority of mice.

In early period (1 month) autoantibodies appear not to all antigens which fact allows a suggestion that immune responses to different brain structures are triggered step-by-step. This may evidence for a stepped character of the brain damage under small-dose radiation. The most sensitive brain structures (glial and nervous cells) are the first to suffer, while less sensitive ones (myelin and oligodendroglia) undergo damage later.

Of particular interest are data obtained as to specificity of autoimmune responses in mice having a 3-month interval after a 6-month radiation exposure. 66 % of this animals reveal autoantibodies to NSE, whereas only 16,7 % show autoantibodies to MBP, this value being lower than that in the group receiving isotopes during 9 months.

Thus, autoimmune responses remain to exist after isotopic exposure and nuclide withdrawal from the blood and brain, acquiring the features of a chain reaction.

Different frequency of autoantibody appearance in the groups of animals receiving and not receiving isotopes testifies to the dynamical character of the process and its relatioship with the brain and immune system injuries. The fact that autoantibodies to NSP were identified not in all but in a part of the animals under test points to the existence of an individual sensivity (threshhold) to inner radiation. It cannot be excluded that such a sensitivity is controlled by histocompatibility gens or by other censor systems.

Considering the reasons why autoantibodies are inavailable in some animals" blood the following assumptions can be made: 1) Autoantibodies are almost entirely bound to the blood-circulating antigens; 2) Autoantibodies are produced through the immune system suppression; 3) There exists either cell or humoral inhibitor to slow down the development of immune responses, and whose nature is to be studied farther on.

To understand more completely the mechanisms of radiation effects on the brain structure and function, we determined the serum content of MBP. The results tell of a wave-like protein content in the blood. After a month of radiation exposure the highest MBP content amounted to 258 ng. Later on the MBP level decreased and remained within 100-123 ng.

The data obtained may be compared to the level of autoantibodies to MBP. In early period (1 month) no autoantibodies to MBP are seen in the animals" blood, although this is a period of the highest MBP concentration. In more prolonged periods there appear autoantibodies which bind and remove the antigens from circulation thereby reducing their content in the blood. It may be suggested that in early periods (1-st month) radionuclides destroy nervous cells most actively. Then the compensatory mechanisms are triggered to prevent further brain damage and antigen outflow into the blood. Both mechanisms are likely to be involved: on the one hand the processes of primary and secondary brain damage are taking place, and on the other hand the compensatory mechanisms are being triggered.

Of special interest seem to be the data on the MBP content in the animals' blood after a 3-month restoration period when the animals received no radionuclides. The MBP content in these animals was found to lower practically to the control values pointing to regenerative processes and destruction intensity decrease.

When determining the NSE content, its level was noticed to grow after the 6-th month of radiation exposure reaching maximum after 9 months. In the group of animals having a 3-month interval after a 6-month Cs-137 consumption this level was lower than in the group exposed to radiation during 6 months but higher than in the control group, this fact being probably indicative of the onset of reparative processes in the brain.

CONCLUSIONS

After 1,3,6 and 9 months of Cs-137 dietary intake 50-60% of experimental animals releaved the availability in the blood of antibodies to the brain structures as well as blood-circulating neuroantigens MBP and NSE, this evidencing for the development of destructive processes in the brain due to incorporated radionucludes.

The antibody level was found to grow gradually and continuously from the 1-st to the 9-th month. However, a 3-month interval after 6 months of Cs-137 intake involves statistically significant decrease of neuroantibody and autoantigen blood levels as compared to the animals fed with Cs-137 without intervals, this testifying to reparative processes in the brain.

Inner radiation disturbs blood-brain barrier permeability, allows the brain transbarrier tissues to contact the immune system thereby enabling a stopped autoimmune process to be developed in the CNS. It follows that autoimmune responses to the brain antigens may prove the existence of the brain organic damage because of inner radiation due to incorporated radionuclides.