The Hematopoietic System of the Acute Radiation Syndrome Reconvalescents in Post-Accidental Period

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Abstract. The state of hemopoietic system has been studied since 1986 up to now in 145 patients who had acute radiation sickness after the Chernobyl accident. We studied clinical, morphofunctional, histological, ultrastructural, biophysical, cultural, cytochemical indexes of the hematopoietic elements. The connection between hemopoietic microenvironment and hemophoiesis state was put up. The realization of the hematological disorders as myelodysplastic syndrome testified the most important problem in future.

1. Introduction

The Chernobyl Accident led to special situation when some people taking part in elimination of its consequences of Chernobyl accident were irradiated in high doses. We are interested in the hemopoietic system reaction among 145 patients with acute radiation sickness (ARS) of different degrees. Some scientific publications show a high sensitivity of hemopoietic tissue to ionizing radiation [1,2,3].

2. Materials and methods

One hundred and five patients after ARS were studied. The morphofunctional, clinical, biophysical, cultural, ultrastructural methods were used. The clinical features, the quantitative and qualitative changes, the ultrastructural organization of blood and bone marrow cells were evaluated. Besides, the colony-forming activity of the progenitor cell in the tissue culture in vitro and the influence of hemopoietic microenvironment on the stromal elements and its role in the forming of hematopoietic pathology were studied.

3. Main results

The dynamic investigation of hemopoietic system state in the patients after ARS I-II degrees showed that in acute period, changes in bone marrow were typical. The myelokaryocytes number varies from 8 to 138 x 10^9/l. The quantity of megakaryocytes in 50 % patients in the first 3-5 days after irradiation stayed normal. In some cases its number decreased to full disappearance. Simultaneously, the karyorrhexis and nuclears' fragmentation of hematopoietic cells were intensified. Also, the number of granulocytes and erythrocytes were decreased and the number of lymphoid elements was increased. In the same time the number of reticular and plasma cells in bone marrow was enlarged. 3-5 days after irradiation the active macrophages with ability to phagocytosis appeared. We found the hypoplastic state of bone marrow in this group of patients by using morphological, histological and ultrastructural methods. The cultural investigations showed changes of ability of hemopoietic elements to colony-forming with predominance of eosinophilic-neutrophilic colony. In the same time there was reduction of stromal elements ability to colony-forming in monoline culture to its disappearance in some cases.

In the first period after irradiation in most of the patients leukopenia, thrombocytopenia, erythrocytosis, leukocytosis and lymphocytosis were found. If in the acute period the qualitative changes (hyper- and hyposegmentation, nuclear fragmentation, karyorrhexis, karyolysis, pyknosis, basophilic cytoplasm, nuclear and cytoplasm vacuolization, bilobal nuclear) were observed in most of the patients, some 30 days later these changes decreased. It was revealed in 30-40 % patients.

Ultrastructural investigations have shown that most of the endothelyocytes are characterized by the modifications of the cells' sizes and forms, the increase of electron density of cytoplasm and other changes.

9 years after the Chernobyl accident in the reconvalescents ARS changes in the hemopoietic system were found. The clinic-laboratory examination of the patients showed more often stable moderate anemia, leukocytosis, lymphocytosis and leukopenia than in the first period after irradiation.. Hypersegmentation, fragmentation of nuclears, the toxical granulation, hair- and basophilia of the lymphocytes cytoplasm, the vacuolization of cytoplasm and nuclears were observed in the blood and bone marrow cells.

We found the decrease of bone marrow cellularity to 10,0 - 13,0 x 10^9/l in some cases of examined groups after myelogram analysis. For the others the number of myelocaryocytes was normal and the hypercellularity was found only in 7 patients. The number of megacaryocytes fluctuated, as a rule, on the level of physiological standard, but the increase of the number of megacaryocytes were with lesser size of nuclear and shape modification. The number of cells with active production of platelets was decreased.

The correlation between the hematopoietic lineages was normal in the most cases in spite of the number of myelocaryocytes which were decreased. In some cases the narrowing of erythroid lineage from 5,5 to 10,5 % took place.

The membrane permeability of blood erythrocytes increased in the investigating group according to the data of osmotic and mechanical resistance.of erythrocytes. The thorning and spherical forms of erythrocytes were found in the peripheral blood of 40 % observed patients.

9 years later the ultrastructural changes of the hemopoietic elements remained the same. The histological investigations showed the predominance of the fat marrow over hemopoietic one with essential fibrosis.

We observed the increase of activity of antibacterial enzymes and decrease of the number PAS-positive lymphocytes in the bone marrow and peripheral blood.

Assessment of functional activity of hemopoietic progenitor cells (CFU-GMdc) was determined in bone marrow by quantity colonies - clones on 1e10 cultivating cells and their morphological analysis. The cloning efficiency of bone marrow in 1986 was low 12,6 + 0,6 for ARS degree I and 9,4 + 2,6 for ARS degree II. Those colonies consisted of blasts, metamyelocytes and maturing neutrophils, but rarely monocytes and macrophages. Eosinophilic and eosinophilic-granulocytic colonies predominated. Presence of eosinophilic's progenitor cells correlated with rising eosinophilic leucocytes in peripheral blood and bone marrow.

Cloning of progenitor cells 5-10 years after accident has shown that independent of the degree of ARS, in 19 patients with ARS (degree I) and 4 patients with ARS (degree II) quantitative changes in colony-forming activity in vivo were 38,5 - 3,6 and 30,0 - 5,4, correspondingly. The average number of colonies in the control was 36,5 + 3,8. Tendency to lowering this index in 5 patients was accompanied by morphological changes manifested by predominance of eosinophilic and eosinophil-neutrophilic colonies.

So, after some years in the majority of cases no significant differences in colony-formation in comparison with control were seen. However, predominance eosinophilic and eosinophilic-neutrophilic colonies in culture of 80 % examined patients was noticed though no eosinophilia in peripheral blood was observed.

The cultural research of stromal progenitor cells showed that the stromal progenitor cell activity varied from normal indexes to total proliferative potential depression. For three cases (ARS of degree I) grew none cluster and colony in the culture after 14 days of the bone tissue cultivation in vitro. The fibroblasts were absent. That testified to the presence of total depression of bone marrow stem cell stromal activity.

The research of paramagnetic centers carried out by using electron paramagnetic resonance method let us find the CU^{2+}- ceruloplasmin level decrease for the reconvalescents of ARS. The methemoglobin paramagnetic signal efficiency was normal and the free radical efficiency was greater than of the control group. The results of bone marrow paramagnetic centers studying (8 patients) appeared very interesting. The research carried out showed that the bone marrow paramagnetic centers efficiency was different from that of blood for stable modifications of peripheral blood (leukocytosis, leukopenia, anemia).

During the observation period we found the development of the hematological disorders after high doses of irradiation: 3 cases of myelodysplastic syndrome.

4. Conclusions

The results of our study show that the hemopoietic system of the reconvalescents ARS remain damaged. The presence of the qualitative and quantitative changes in the hematopoietic elements is acknowledged. The connection between hemopoietic microenvironment and hemopoiesis state was put up. The realization of the hematological disorders as myelodysplastic syndrome testified the importance of this problem in future.

References

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