Keywords: stem cells; radiation; leukemia; Chernobyl

Abstract. Studies performed at RCRM have shown that hematopoietic and immune systems’ reconstitution after irradiation depends greatly on the functional abilities of the stem cells. Subset analysis and expression of CD34+ antigens on bone marrow and peripheral blood cells were studied in Chernobyl accident clean-up workers including patients with leukemia and myelodysplasia and patients exposed to the natural levels of irradiation. In myelodysplasia the elevation of early CD34+ cells was detected in bone marrow and peripheral blood. In leukemia the CD34+117+38- primitive progenitor cell counts were elevated mainly in patients with proliferation of poorly differentiated cells while in ALL’s the CD34+ counts were smaller. Circulating HSC and progenitors after radiation exposure in a wide range of doses have are preserved in a number and with proliferation potencies sufficient for the onset of clonal proliferation. In AML FLT3 mutations are the most abundant single-gene mutations. There is no difference in prevalence of FLT3 mutations in groups of radiation-associated and spontaneous AML cases. LOH/deletions at 5q and/or 7q and 7p tend to be more frequent in radiation-associated AML cases. Bone marrow and bone tissue microenvironment plays a key role in normal and neoplastic HSC changes. Differentiation to B-lineage isn’t changed and is associated with B-cell compartment growth.

1. Introduction

The main property of hematopoietic stem cells (HSCs) is the ability to balance self-renewal versus differentiation cell fate decisions to provide sufficient
primitive cells to sustain hematopoiesis by the asymmetric cell division (Ho, 2005). The target of cell-transforming mutations is still unknown. Because normal stem cells and leukemic stem cells (LSC) share the ability to self-renew, as well as various developmental pathways, it has been postulated that LSCs are HSCs that have become leukemic as the result of accumulated mutations. LSCs could derive from more committed progenitors or even a differentiated mature cell, which would have first to reacquire the self-renewal capacity before accumulating additional mutations (D. Bonnet, 2005). Several questions appear to be addressed: are there any specific SC in leukemia and what makes HSC leukemic; what is the specificity of these SC and can we distinguish them from normal cells; could SC in leukemia in differentiate to normal hemopoietic progenitors; could leukemic HSC or their progeny de-differentiate to non-hemopoietic neoplastic clones; what is the place of ionizing radiation in this process?

Leukemia holds a special place in the study of radiation-related cancer because bone marrow is one of the tissues most sensitive to the carcinogenic effect of ionizing radiation, radiogenic leukemia has the shortest latent period among radiation-induced cancers, and its appearance suggests that solid tumors may follow. A retrospective case-control study of ionizing radiation and leukemia that was conducted in a cohort of 110,645 male Ukrainian radiation workers involved in cleanup work following the accident at the Chernobyl nuclear power plant in northern Ukraine which occurred on April 26, 1986 has demonstrated the excess of leukemia radiation risks at doses higher that 100 mSv (Romanenko et al., 2006) 8-14 years after the radiation exposure. Similar data was obtained in Russia (Ivanov et al., 1997). At high dose level leukemia rates are increased.

The aim of this study was to explore if the HSC and progenitor cells after radiation exposure at different levels have the self-renewal capacity needed for leukemia induction and do HSC undergo subsequent mutation process?

2. Patients and Methods

The study was performed in patients exposed to ionizing radiation after Chernobyl accident. Comparison groups included patients and healthy individuals exposed to the natural radiation levels. Control group included healthy volunteers who resided in Kyiv since Chernobyl accident Distribution by diagnosis is presented at table 1. Investigated persons were at the age of 43-72 (mean±SD for the exposed group: 52,3 ± 10,1 yrs; for control group- 46,3 ± 11,3 yrs). All studied persons participated by informed consent. Peripheral blood and bone marrow samples were obtained by a standard procedure (National. Committee for Clinical Laboratory Standards, 1991). Flow