Increased Incidence of Lymphosarcoma in Long-Term Murine Survivors of Lethal Radiation: A Classification of Subtypes.

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Residual bone marrow damage (RBMD) persists for years following exposure to radiation and is thought to be due to decreased self-renewal of hematopoietic stem cells (HSC). We previously examined RBMD in murine survivors of lethal radiation modeling a terrorist event [800cGy total-body irradiation (TBI)]. We reported severely deficient HSC potential up to 20mo post-TBI compared to non-TBI age-matched controls, evidenced by minimal engraftment skewed to myeloid cells. CBC and BM cellularity were decreased in TBI mice, most dramatically in old age (>16mo). The percentage of some hematopoietic progenitors was consistently increased in TBI mice (~1.4x higher than non-TBI) possibly due to an increased cell cycling rate compared to non-TBI cells. Of interest, we now report the occurrence of a thymic mass developing in 13-24% of TBI mice 2-19 months post-TBI, compared to <1% of non-TBI. We characterized the Lymphosarcoma into the following groups based on the St. Jude pathology sub-classification: Diffuse Lymphosarcoma involving multiple organs, Thymic lymphoma (usually associated with thymic and around the heart), Lymphosarcoma (potentially starting in the spleen and peri-pancreatic lymph nodes (Ab=abdomen)), and follicular lymphoma seen as a diffuse proliferation of lymphocytes in the white pulp area in the spleen. Thymic lymphomas were the most common, followed by Lymphosarcoma (Ab), follicular lymphoma (restricted to white pulp area in the spleen) and diffuse Lymphosarcoma. Immunostain markers revealed the thymic lymphomas were from T-cell lineage and the abdominal Lymphosarcoma were mainly from B-cell lineage. A few mice had disease involving the bone marrow. Taken together, these data suggest that the increased cycling among primitive hematopoietic cells in survivors of lethal radiation may contribute to stem cell exhaustion and subsequent RBMD, as well as predispose survivors to hematopoietic neoplasias.

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