Expansion of CD8+/Perforin+ T-Cell Predicts Response to Cyclosporin A Therapy in Patients with Erythroid Hypoplasia/Aplasia

Hideaki Nitta1, Yuka Harada1, Hideo Hyodo1, Akiro Kimura1, and Hironori Harada1
1) Department of Hematology and Oncology, Division of Clinical Research, Research Institute for Radiation Biology and Medicine, Hiroshima University 2) Division of Radiation Information & Registry, Research Institute for Radiation Biology and Medicine, Hiroshima, Japan

Abstract
Erythroid hypoplasia or aplasia is a hematological condition observed in poorly differentiated lymphoid malignancies and a rare form of myelodysplastic syndromes (MDS). However, the pathogenesis of erythroid hypoplasia/aplasia has been not fully characterized. To clarify the pathological role of the T cells, we analyzed the T cell subsets of bone marrow (BM) or peripheral blood (PB) mononuclear cells (MNCs) and therapeutic responses in a total of 22 patients with erythroid hypoplasia/aplasia. Interestingly, CD8+/Perforin+ T cells were significantly increased in the cyclosporin A (CSA) responders compared with those in non-responders. It is suggested that the CD8+/Perforin+ T cell population may have some potential function in the pathogenesis of erythroid hypoplasia/aplasia. Our results show that the expansion of CD8+/Perforin+ T cells predicts response to CSA therapy in patients with erythroid hypoplasia/aplasia. The CD8+/Perforin+ T cell subset in this disease entity could be a useful marker to CSA therapy.

Background
Erythroid hypoplasia or aplasia is a hematological condition observed in poorly differentiated lymphoid malignancies and a rare form of myelodysplastic syndromes (MDS). However, the pathogenesis of erythroid hypoplasia/aplasia has not been fully characterized. Patients with erythroid hypoplasia/aplasia have certain characteristics: thrombocytopenia, immunologic abnormalities, and successful immunosuppressive therapy (such as cyclosporin A (CSA) and/or antithymocyte globulin (ATG)). Thus, we may regard erythroid hypoplasia/aplasia as an immunologic disease entity. However, the pathogenic mechanisms of erythroid hypoplasia/aplasia have not been elucidated. To elucidate the T-cell role in MDS, we analyzed the T-cell subsets and therapeutic responses in patients with erythroid hypoplasia/aplasia.

Methods
Characteristics of patients with erythroid hypoplasia/aplasia

Results
Comparison of CSA responders and non-responders

In patients in whom the proportion of CD8+/Perforin+ T cells was expanded (CSA responders), the proportion of CD8+ T cells as well as CD8+ T cells in PB and BM were significantly higher than in patients in whom the proportion of CD8+/Perforin+ T cells did not expand (CSA non-responders).

Immunohistological analysis of proliferating T cells in bone marrow sections revealed that CD8+/Perforin+ T cells showed a good response to CSA therapy.

Discussion
Among 22 patients with erythroid hypoplasia/aplasia, 10 patients were MDS with erythroid hypoplasia/aplasia (3 patients, 1 Cyclosporin A-associated MDS, and 2 aleukemic response in CSA therapy for 6–48 weeks). The results of the immunohistological analysis demonstrated that CD8+/Perforin+ T cells were significantly increased in the bone marrow of patients with CSA responders compared with non-responders. CSA-induced suppression of CD8+/Perforin+ T cells was associated with a better clinical response in CSA responders. In patients with non-expanded CD8+/Perforin+ T cells, no significant changes were observed in the bone marrow of patients with CSA non-responders.

References