Cureus

Open Access
Poster

Lost and Found: Therapeutic Implications of Bone Marrow as Harbor for Missing T-cells in Glioma

Peter E. Fecci [1] , Christina Chen [2]

1. Massachusetts General Hospital 2. Harvard Medical School

Corresponding author: Peter E. Fecci, pfecci@partners.org

Categories: Neurosurgery
Keywords:

How to cite this poster
Fecci P E, Chen C (2012) Lost and Found: Therapeutic Implications of Bone Marrow as Harbor for Missing T-cells in Glioma. Cureus 4(10): e493.

Abstract

Lost and Found: Therapeutic Implications of Bone Marrow as Harbor for Missing T-cells in Glioma Introduction The success of glioblastoma immunotherapy has been limited by tumor-provoked immune dysfunction. Peripheral blood CD4+ T-cell defects include marked lymphopenia and disproportionately high frequencies of regulatory T-cells (Tregs). Determining the etiology to these is essential; we thus sought fuller characterization of glioblastoma-induced alterations to the T-cell compartment as well as strategies for reversal. Methods Blood, bone marrow, spleens, lymph nodes, and tumors of mice bearing gliomas or other cancers were characterized using 8-color flow cytometry. Serum and bone marrow supernatants were analyzed by ELISA. For survival studies, PBS, G-CSF, anti-CTLA-4 monoclonal antibody, or a combination were administered to tumor-bearing mice beginning on Day 4 following tumor implantation. All immune compartments were analyzed, and Kaplan-Meier survival curves were calculated. Results The bone marrow of mice bearing intracranial glioma was uniquely characterized by a 6-fold naïve (CD4+CD44loCD62Lhi) T-cell expansion compared to control mice. Additionally, 20-30% of the CD4+ lymphocytes in the bone marrow of these glioma-bearing mice were Tregs. No evidence of bone marrow metastasis was found, and the phenomenon was CXCR4/CXCL12-independent. Intraperitoneal G-CSF administration reversed bone marrow T-cell accumulation and increased numbers in the peripheral blood. Combining G-CSF with anti-CTLA-4 monoclonal antibody was synergistic, conferring long-term survival in mice with established gliomas. Conclusions Immunologically recapitulative murine models suggest T-cell re-allocation to the bone marrow in association with glioblastoma-associated lymphopenia. G-CSF administration reversed this phenomenon and re-distributed T-cells to the circulation, where concomitant activation by anti-CTLA-4 precipitated long-term survival in a model of established intracranial glioma. These findings support novel therapeutic approaches.

Open Access
Published 10/12/2012

65