Effect of Transplanted Bone Marrow Cells in Mice Model with Carbon Tetrachloride Induced Liver Fibrosis

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Backgrounds/Aim: Recent reports have shown the capacity of the bone marrow cells (BMC) to differentiate into a variety of non-hematopoietic cell lineages. Albeit there are a lot of controversy, these results indicate that the BMC is an attractive cell source for regenerative medicine compared with tissue-specific stem cells. The aim of this study is to reveal the fate and effect of transplanted bone marrow cells in mice model with carbon tetrachloride (CCL4)-induced liver fibrosis. Materials and Methods: Six-week-old female C57BL6 mice were treated with 1 ml/kg CCL4 dissolved in corn oil (1:1) twice a week for 4 weeks. At one day (24 hours) after the 8th injection of CCL4, 1 x 10^6 green fluorescent protein (GFP)-positive BMCs or same volume of saline as a control (described also as mice treated with CCL4 alone) were injected into the tail vein as described previously. Mice continued to be treated with CCL4. After 1, 2, 3, or 4 weeks, mice were sacrificed to assess engraftment of GFP-positive BMCs into liver and the extent of liver fibrosis. The identification of transplanted bone marrow cells was observed with histological study and polymerase chain reaction. For the evaluation of fibrosis, picro-sirius red staining was performed and fibrotic area, was assessed by computer-assisted image analysis with Meta-Morph software (Universal Imaging Corporation, Downingtown, PA). Results: Five weeks after CCL4 injection, liver fibrosis was seen. There was no mortality during experimental period. Transplanted BMCs were visualized in immunohistochemical staining using anti-GFP antibody and in PCR product of liver tissue. The number of GFP-positive cells gradually increased, spreading into the liver lobules 1-4 weeks after BMC transplantation. Transplanted BMCs were seen along with the collagen fibers, and quantitative image analysis of liver fibrosis indicated that the area of liver fibrosis after BMC transplantation was significantly less than that of control group with sirius red staining (p<0.05). Conclusion: BMCs transplanted into mice with CCL4-induced liver fibrosis might serve as regeneration source and reduce liver fibrosis. Human clinical trial to evaluate these effect is warranted.

Korean: Bone marrow, Cell transplantation, Liver cirrhosis, Stem cell

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