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Immunomodulatory effect of bone marrow mesenchymal stem cells on T lymphocytes in patients with decompensated liver cirrhosis

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ABSTRACT. We explored the immunomodulatory effects of bone marrow mesenchymal stem cells (BMSCs) on peripheral blood T lymphocytes in patients with decompensation stage, hepatitis B-associated cirrhosis. MSCs from nine patients were analyzed by flow cytometry. Peripheral blood lymphocytes were isolated for fluorescent staining. Following stimulation by phytohemagglutinin (PHA), peripheral blood lymphocytes were co-cultured with BMSCs in serum and divided into four groups: (1) BMSC + lymphocyte + PHA contact culture group; (2) BMSC + lymphocyte + PHA non-contact culture group; (3) lymphocyte + PHA positive control group; and (4) lymphocyte-only negative control group. Lymphocyte proliferation and frequencies of $CD4^+CD25^+CD127^-$ Tregs and $CD4^+CD8^-IL\text{-}17^+$ (Th17) cells were detected. Cell proliferation in groups 1 and 2 declined compared with group 3 ($P < 0.01$), and was notably higher than in group 4 ($P < 0.01$). $CD4^+CD25^+CD127^-$ Tregs frequencies in groups 1 and 2 were higher than in groups 3 and 4. In an intra-group comparison before and after culture, Th17 cell frequencies in groups 1 and 2 were higher than in group 4 ($P < 0.01$), but lower than in group 3 ($P < 0.01$). The Treg/Th17

ratio in groups 1 and 2 increased ($P < 0.01$), but did not change significantly in groups 3 and 4 ($P > 0.05$). In a comparison between groups after culture, the Treg/Th17 ratio in groups 1 and 2 increased more than in groups 3 and 4 ($P < 0.01$). BMSCs from cirrhotic patients can inhibit the proliferation of peripheral blood T lymphocytes, upregulate the expression of $CD4^+CD25^+CD127^-$ Tregs, and improve Treg/Th17 imbalance. The mechanism by which this takes place may be associated with immunomodulatory effects induced by the secretion of soluble factors.

Key words: Hepatitis B; Hepatic cirrhosis; Th17; Treg/Th17; Bone marrow mesenchymal stem cells; Treg

