28th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Madrid, Spain
21 – 24 April 2018

P0046 A novel therapeutic approach to protect mice against herpes simplex virus type 1 infection using mesenchymal stem cells

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Background: Herpes simplex virus (HSV1) is widely spread in human population. The diseases caused by HSV1 are characterized by a wide range of clinical manifestations. Cell therapy with the use of mesenchymal stem cells (MSC) is a novel approach to treatment of various diseases. Data on the attempts to use MSC in antiviral therapy are scarce or absent. Our objective was to evaluate immunoregulatory and therapeutic activities of MSC in a mouse model of HSV1 infection.

Materials/methods: MSC culture was initiated from bone marrow of DBA mice. 3 groups of 10 DBA mice were injected with HSV1 (20 LD_{50}) intraperitoneally. After 4 and 24h the mice were given tail vein injection of saline (group 1, control, HSV1+saline) or $5x10^5$ MSC per animal (group 2, HSV1+MSC+). Group 3 (HSV1+ACV+) mice received acyclovir (100 µg, twice daily, intraperitoneally) for 3 days. 10 uninfected mice (group 4, HSV1-MSC+) were given MSC injections as in group 2. After 7 days anti-HSV1 antibodies were determined in serum by ELISA and microneutralization test. T-cell response was examined in blast transformation test. Serum levels of IL-6, IFN-γ and TNF-α were measured by ELISA.

Results: Survival and mean lifespan in group 2 mice (HSV1+MSC+) were significantly higher than in the control: 70% vs 20% and 11.3±0.13 vs 6.2±0.31 days, $P<0.05$, respectively. In group 3 (HSV1+ACV+) these parameters were 40% and 9.5±0.25 days, respectively. Anti-HSV1 antibody and virus-neutralizing antibodies titers were significantly higher in group 2 (HSV1+MSC+) than in control group 1 (1:11200 vs 1:4267 and 1:625 vs 1:50, respectively, $P<0.05$). The number of blasts in splenocyte population was significantly higher in group 2 than in groups 1 and 3: 514±60.2 vs 21.3±7.6 and 62.7±15.3, respectively, $P<0.05$). Serum IL-6 level in group 2 (HSV1+MSC+) was significantly lower than that in control group 1: 0 pg/ml vs 84 pg/ml, while INF-γ concentration was higher: 1114 pg/ml vs 44 pg/ml, $P<0.05$. No statistically significant differences were detected in TNF-α level.

Conclusions: These results show that anti-HSV1 therapy based on MSC leads to production of virus-neutralizing antibodies, enhances T-cell proliferation, increases IFN-γ level and protects 70% mice against lethal HSV1 infection.