Effectiveness evaluation of dendritic cell immunotherapy for osteosarcoma on survival rate and *in vitro* immune response

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ABSTRACT. The aim of this study was to investigate the effects of dendritic cell (DC) therapy in osteosarcoma. Bone marrow DCs from Wistar (allograft group) and Sprague Dawley (SD) (homograft group) rats were electrically fused with the SD-derived osteosarcoma cell line UMR106 to generate a DC-osteosarcoma fusion (DOF) tumor vaccine, which was co-incubated with SD T lymphocytes to stimulate T cell proliferation. CD8+ and CD4+ cell percentages were measured by flow cytometry; tumor-cytotoxic effects of cytotoxic T lymphocytes (CTLs) were measured by the MTT assay. Active immunotherapy was applied to SD osteosarcoma model rats via subcutaneous injection of the tumor vaccine. Significant potentiation of T lymphocyte proliferation was observed in both groups. In the homograft group, the CD8+/CD4+ ratio was elevated to 78.2 from 55.1% after stimulation ($P < 0.05$) whereas the CD4+ cell percentage was reduced from 61.3 to 21.2% ($P < 0.05$). Similarly, in the allograft group the CD8+ and CD4+ cell percentages significantly increased (33.8 to 69.6%) or decreased (61.3 to 28.1%)

after stimulation, respectively ($P < 0.05$). The preferential homograft group response was not significant ($P > 0.05$). Induced UMR106-specific CTLs showed a significantly higher tumor-cytotoxic effect after stimulation ($P < 0.05$). After DOF active immunotherapy, tumor bodies displayed atrophy or disappearance, leading to higher survival times and rates (60 and 70% in the allograft and homograft groups) ($P < 0.05$). This study demonstrated that osteosarcoma immunotherapy using a DC-fused tumor vaccine can effectively stimulate T lymphocyte proliferation and induce the tumor-cytotoxic activity of CTLs.

Key words: Dendritic cells; Immunotherapy; Cytotoxic T lymphocytes; Osteosarcoma

