THE COMBINATION OF ANTITUMOR VACCINE AND LOW DOSES OF DOXORUBICIN AS AN EFFECTIVE METHOD AGAINST TUMOR IMMUNOSUPPRESSION

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Aim: Combined therapy based on dendritic cells (DC) and low-dose chemotherapy is being intensively investigated worldwide. The use of low-dose chemotherapy, such as cyclophosphamide, reduces the number of T-regulatory cells, which in turn decreases the suppression of the immune system of cancer patients. The aim: to investigate the influence of combined immunotherapy on T-regulatory component of the immune system in murine sarcoma-37 model.

Methods: In experimental investigation 120 CBA mice have been involved. Sarcoma-37 was injected intramuscularly at lethal dose (2*10⁶ cells per animal). Doxorubicin was injected intraperitoneally 5 times in metronomic regimen according to the two schemes: 0.2 mg/kg or 2 mg/kg on the 7th day after tumor transplantation with interval of 1 day and 3 days, respectively. DC vaccines were administered intravenously 3 times on day 4 after the chemotherapy in 3 day interval.

Results: We have found that both of the proposed chemoimmunotherapy schemes had a significant antitumor and immunomodulating effect. Significant decreasing of primary tumor volume in both animal groups which received combined therapy compared with the control has been found (p<0.01). We have shown that administration of DC vaccine and doxorubicin at a concentration of 0.2 mg/kg decrease FoxP3 mRNA expression level in spleen cells in 1.7 times (p=0.03) compared with the control group. Moreover, the administration of this combined therapy decrease dTGF-β mRNA expression level in spleen cells by 1.8 times (p=0.028) compared with the control group. This data has shown that the chemoimmunotherapy decreases the T-regulatory cells suppressive effect on the animal’s immune system.

Conclusions: Low-dose chemotherapeutics decrease the tumor suppression on immune system and enhance the antitumor effect of DC-based immunotherapy. These investigations form the basis to a new multimodality treatment in cancer patients.

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