

ONCOLOGY

Antitumor Activity of Specific Immunotherapy with Mucin Containing CA 125 Antigen in Mice with CaO 1 Ovarian Carcinoma

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Experiments in CBA mice with transplanted CaO 1 ovarian carcinoma possessing common antigenic determinants with human ovarian carcinoma showed that specific immunotherapy with mucin containing CA 125 antigen inhibited tumor growth by 60% and prolonged animal lifespan by 40-60% in comparison with the control. The correlation coefficient between the tumor size and antibody titer after injection of mucin was -0.4 for IgM and -0.6 for IgG. Titration of IgG may be used for monitoring of the efficiency of specific immunotherapy.

Key Words: CA 125 antigen; specific immunotherapy; CaO 1 murine ovarian carcinoma

Adequate models for studies of specific immunotherapy of malignant tumors help to precisely evaluate their efficiency under experimental conditions and predict their clinical efficiency. In experiments, specific immunotherapy leads to cure of 70% animals with tumors bearing the gene encoding human carcinoembryonal antigen, while in patients with melanoma immunotherapy prolongs the lifespan by no more than 20-25% [2,3], probably because human antigens are foreign and hence more immunogenic for experimental animals. In order to reduce the effects of interspecies barriers in studies of antitumor activity of specific immunotherapy with mucin containing CA 125 glycoprotein, we searched for an experimental tumor possessing common antigenic determinants with CA 125 antigen, expressed in the majority of patients with ovarian and breast cancer. In previous studies with autoantibodies to CA 125 antigen we demonstrated common antigenic determinants of human ovarian carcinoma and murine CaO cells [1]. In this study we

evaluated activity of specific immunotherapy with mucin containing CA 125 antigen in mice with pseudomucinous CaO ovarian carcinoma and determined criteria for assessing the efficiency of this immunotherapy.

RESULTS

Female CBA mice aged 2-3 months were used. Mouse CaO 1 cells were transplanted subcutaneously (10^6 cells in 0.3 ml medium 199). Mucin containing CA 125 antigen was injected in a dose of 100 μ g/mouse on days 1, 2, 3, 10, and 17. Albumin was injected in a dose of 100 μ g/mouse according to the same scheme. Therapeutic efficiency of mucin containing CA 125 antigen was evaluated by inhibition of tumor growth and prolongation of the lifespan of animals receiving immunotherapy in comparison with mice treated with albumin and untreated animals. Tumor size was measured on days 14, 18, and 21 after transplantation. The data were processed using Fisher-Student method, the differences were considered significant at $p < 0.05$.

Titer of antibodies to mucin containing CA 125 antigenic determinant was measured by enzyme im-

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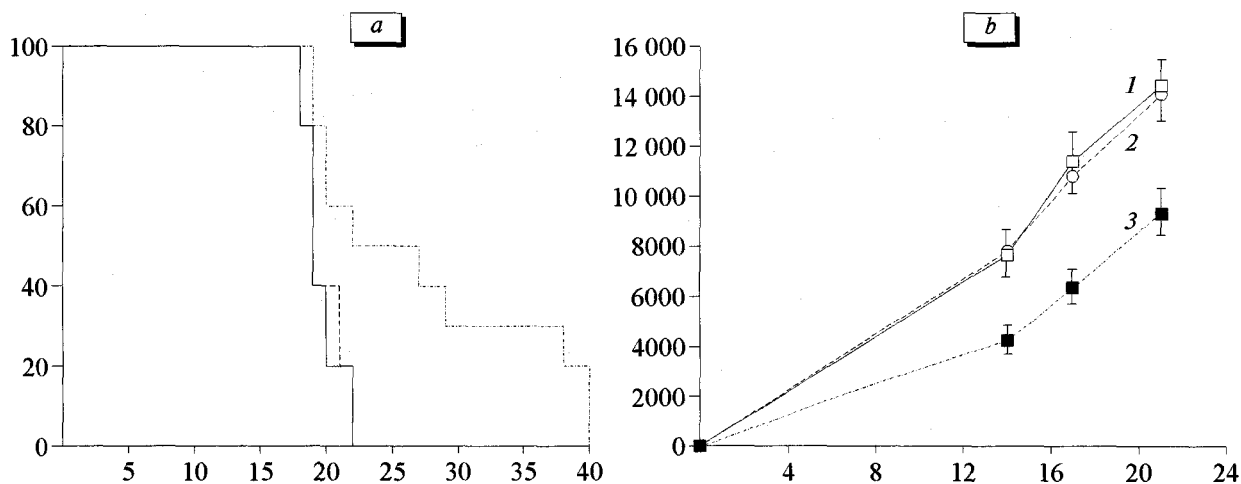


Fig. 1. Effect of immunotherapy with mucin containing CA 125 antigen on the lifespan (a) and tumor size (b) in mice with CaO 1 ovarian carcinoma. 1) control; 2) albumin; 3) therapy with mucin containing CA 125 antigen.

munoassay on day 16 after tumor transplantation, *i. e.*, after the 4th injection of mucin. Each group consisted of 10 animals.

RESULTS

Injection of mucin containing CA 125 antigen to mice with transplanted CaO 1 carcinoma prolonged the lifespan by 40-60% in comparison with animals injected with albumin and untreated controls (Fig. 1, a). The mean lifespan of animals receiving specific immunotherapy was 26.8 ± 0.9 days *vs.* 19.3 ± 0.5 and 19.6 ± 0.6 days in animals injected with albumin and untreated controls, respectively.

Specific immunotherapy inhibited tumor growth by 60% in comparison with albumin group and untreated controls (Fig. 1, b). For evaluating the immunogenicity of antigens and antitumor activity associated with it, titer of antibodies to mucin containing CA 125 antigen was determined. The correlation coefficients between the tumor size and IgM and IgG titers were -0.4 and -0.6 (Fig. 2), respectively, *i. e.* which implies an inverse correlation between these parameters.

These results indicate that injection of mucin containing CA 125 antigen to mice with CaO 1 carcinoma possessing common determinants with human ovarian carcinoma cells leads to production of antitumor antibodies inhibiting tumor growth. Such specific immunotherapy may be effective in the treatment of tumors expressing CA 125 glycoprotein, *e. g.*, ovarian carcinoma and breast cancer [4]. Predicted prolongation of the mean lifespan is 40-60%. The efficiency of specific immunotherapy with mucin containing CA 125 antigen can be monitored by IgG titer. In humans, the correlation coefficient between tumor size and antibody titer will be higher because of numerous common antigenic determinants of the injected antigen and

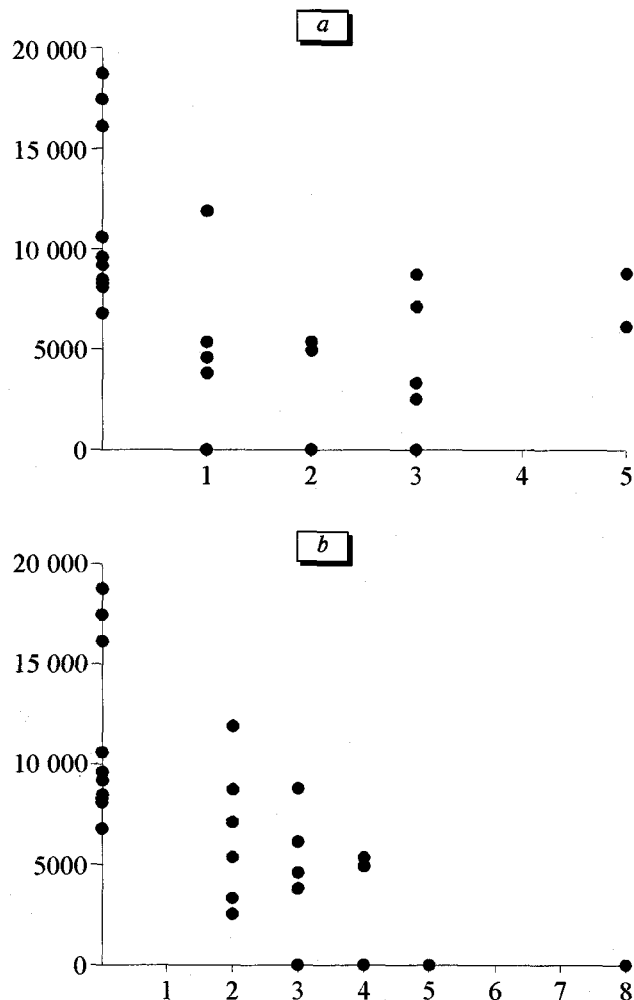


Fig. 2. Correlation between tumor size and specific antibody titer in mice with CaO 1 ovarian carcinoma after immunotherapy with mucin containing Ca 125 antigen. IgM (a), IgG (b).

tumor cells. Further, in particular, toxicological studies are required to elucidate the possibility of clinical use of mucin containing CA 125 antigen.

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