ACTION OF ANTILYMPHOCYTIC PREPARATIONS ON SURVIVAL AND GROWTH OF ALLOGENEIC TUMORS IN MICE

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Transplantable cancer of the forestomach (strain PRZh) obtained and transmitted by passage through mice of line CC57Br did not develop when transplanted in CBA mice. However, injection of antilymphocytic serum or antilymphocytic globulin leads to survival and growth of the allogeneic tumor, and the dynamics of its growth during the first weeks after transplantation is the same as that of growth of the tumor in a syngeneic system.

Although antilymphocytic sera (ALS) have frequently been used in experiments on rodents to study homotransplantation of the skin [3, 7] and other organs, including the kidneys and heart [5, 8], only a few investigations have been made of the action of ALS on the growth of allogeneic tumors [4, 6, 9].

The object of the present investigation was to study the ability of ALS to depress transplantation immunity, and specifically to inhibit the rejection of a tumor transplanted in mice of another line.

EXPERIMENTAL METHOD

A transplantable squamous-cell carcinoma of the forestomach (strain PRZh) obtained from donor mice of line CC57Br, transplanted into CBA mice which differ from the donors in the H2-locus of tissue incompatibility, was used as the experimental model. The strain PRZh was obtained initially from a tumor induced in CC57Br mice by a carcinogen [2], and subsequently maintained in mice of the same line by the group of tumor strains (under the direction of E. M. Shmaeva of the Institute of Experimental and Clinical Oncology).

The ALS was obtained by immunizing rabbits or a horse 3 or 4 times with a mixture of lymphocytes isolated from the spleen, thymus, and lymph glands of noninbred mice. The sera were heated at 56°C and adsorbed with mouse erythrocytes until complete disappearance of the hemagglutinins. Whole ALS or the immunoglobulin fraction (ALG) isolated by salt fractionation [1] was used in the work. The titer of the preparations of rabbit ALS in the lymphagglutination reaction were 1:160-1:640, and in the cytotoxic test 1:300-1:2560. The titer of horse ALG was 1:640-1:1280 and 1:128-1:5120 respectively.

Three groups of mice, with 7-10 animals in each group, formed each series. Group 1 was the syngeneic control: CC57Br mice not receiving ALS, group 2 was the allogeneic control: CBA mice, likewise not receiving ALS, and group 3 was the experimental group: CBA mice receiving ALS as described below. CBA mice weighing 16-18 g received an intraperitoneal injection of ALS or ALG in a dose of 10 mg protein per mouse on 3 occasions: one day before, on the same day, and on the day after transplantation of the tumor. The technique of transplantation consisted of injection of a suspension of the tumor cells in physio-

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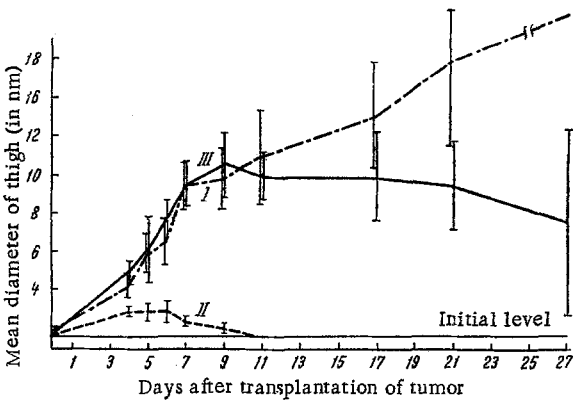

Fig. 1. Dynamics of tumor growth reflected in change in mean diameter of thigh.

TABLE 1. Effect of ALS on Development of Allogeneic Tumor in Mice on 11th Day after Inoculation

	Line of recipient mice	Treatment with ALS	Number of mice	Number of mice with developing tumor	
				abs.	%
1	CC57Br	–	19	19	100
2	CBA	–	20	0	0
3	CBA	+	38	36	95

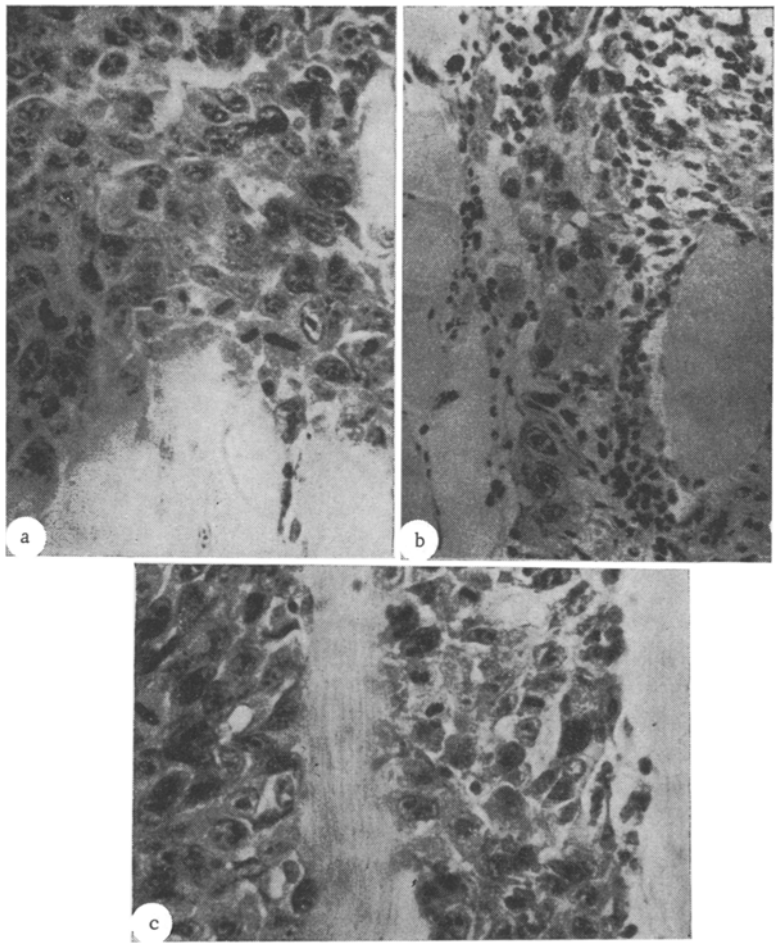

Fig. 2. Histological picture of tumors and surrounding tissues in syngeneic control (a), allogeneic control (b), and experiment (c) on 11th day after transplanation (400 ×). Explanation in text.

logical saline into the fermoral muscles. Experiments on the lines described were repeated 7 times. One index of tumor growth was measurement of the mean diameter of the thigh at the site of inoculation of the tumor. In addition, at different times after transplantation of the tumor the transplant and surrounding tissues in the experimental and control series were examined histologically by the usual method. Numerical results were analyzed by Student's method.

EXPERIMENTAL RESULTS

All the experiments gave consistent results, so that the mean results of 7 experiments, characterizing growth of the tumor in the mice of the 3 groups mentioned above, are given in Fig. 1 and Table 1. The graph showing growth of the tumor in Fig. 1 demonstrates a marked increase in the mean diameter of the thigh in the syngeneic control (group 1), starting from the 4th day after inoculation and continuing until the 25th-27th day. Correspondingly, the histological picture of the tumor (Fig. 2a) indicates active proliferation of its cells, groups of which infiltrate into surrounding muscle bundles; meanwhile no signs of lymphocytic infiltration of the tumor or of the contiguous muscle could be seen.

In the mice of group 2 (allogeneic control) the diameter of the thigh increased slightly until the 5th-6th day and then began to fall rapidly, to reach its initial level by the 11th day. Histological examination of the thigh muscles at the site of innoculation of the tumor confirmed that in 100% of cases the tumor, allogeneic to line CBA, after a short period of growth underwent regression and rejection of the allograft type (Fig. 2b). On the 11th day all that remained of the tumor was a few severely damaged cells showing no evidence of proliferation. Abundant, mainly lymphocytic, infiltration was observed in the surrounding muscles and connective tissue, and there was an active macrophage reaction at the periphery of the groups of tumor cells.

In CBA mice prepared by injection of ALS (group 3) the rate of growth of the tumor during the first 11 days was not significantly different from its rate of growth in the syngeneic control (Fig. 1). However, starting from the 11th day, in some mice the tumors gradually underwent regression. After 1 month tumors were observed only in half of the animals of this group. Nevertheless, in individual mice the tumor remained for more than 2 months.

A histological section through the tumor in a mouse of this group taken on the 11th day after inoculation (Fig. 2c) shows the picture of a growing squamous-cell nonkeratinizing carcinoma of solid type with a large number of mitoses, invading the surrounding muscle tissue, i.e., essentially the same as in the syngeneic control (Fig. 2a).

The investigation thus showed that transplantable carcinoma of the forestomach (strain PRZh) obtained and maintained by passage through mice of line CC57Br will not develop if transplanted into CBA mice. However, injection of ALS or ALG leads to survival and growth of the allogeneic tumor, and the dynamics of its growth in the first weeks after transplantation are indistinguishable from those of growth of the tumor in a syngeneic system, i.e., in CC57Br mice.

This disturbance of the immune response to an allogeneic tumor transplant in CBA mice treated with ALS can be used as an experimental model of suppression of transplantation immunity.

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