EFFECT OF ASITES FLUID ON GROWTH OF EHRLICH'S TUMOR AND LEWIS CARCINOMA

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KEY WORDS: ascites fluid; humoral tumor factors; inhibition of tumor growth.

The concept of concomitant immunity can be taken to mean interaction between several tumors in the body. The effect of one tumor node on another may be specific. For example, during transplantation of two identical tumors separated by an interval of a few days, the second tumor will grow more slowly as a result of preliminary immunization of the host during development of the first tumor [2, 3]. If several tumor nodes of the same or different origin are present in the body, nonspecific interaction may take place, when the larger tumor can inhibit growth of the smaller tumors. In this case the deciding condition of manifestation of an inhibitory action of one tumor node on another is their linear size [4]. It can be tentatively suggested that this inhibitory action is mediated through humoral factors secreted by the tumor. Some such phenomenon may perhaps lie at the basis of generalization of the tumor process when, for example, growth of metastases was observed after surgical removal of the primary tumor. Incidentally, the mechanism of this nonspecific inhibitory action of one tumor node on another has not hitherto been studied.

The aim of this investigation was to create a model system to record inhibition of tumor growth under the influence of humoral factors in vivo. With such a model system it would be possible to study interaction between tumor nodes in vivo and to explain the mechanisms of generalization of the tumor process.

EXPERIMENTAL METHOD

Male (CBA × C57BL/6)F_1 hybrid mice and C57BL/6 mice weighing 25-27 g were obtained from the "Stolbovaya" nursery, Russian Academy of Medical Sciences. Ehrlich's ascites tumor (ELD subline, from the Tumor Strain Bank, All-Union Oncologic Scientific Center, Russian Academy of Medical Sciences) was transplanted intramuscullarly in a dose of $1 \cdot 10^6$ cells per mouse in 0.1 ml medium 199. Lewis lung carcinoma (LL, from the same tumor strain bank) was transplanted intramuscularly in a dose of 0.1 ml of a suspension of 1 g tumor material in 10 ml medium 199 per mouse Biological fluids (BF) comprised C-I – ascites fluid obtained fran animals with ELD ascites tumor on the 10th day after transplantation; C-II – a freeze-dried preparation from a dialysate of ELD tumor cells, obtained by the method described for transfer factor [1]. The freeze-dried preparation was standardized relative to absorbance at wavelengths of 190 and 260 nm, ΔA_{190nm} = 2.9 relative units (r.u), ΔA_{260nm} = 3.3 r.u. The measurements were made on a Hitachi V-2000 spectrophotometer (Japan). BF C-I and C-II did not contain cells and were used in a syngeneic system. BF C-I and C-II were injected intraperitoneally in a volume of 0.8 ml 24 and 48 h after transplantation of the tumor. Animals of the control groups were given an intraperitoneal injection of the same volume of physiological saline The dimensions of the tumors were measured for 3 weeks. The volume of the tumors,

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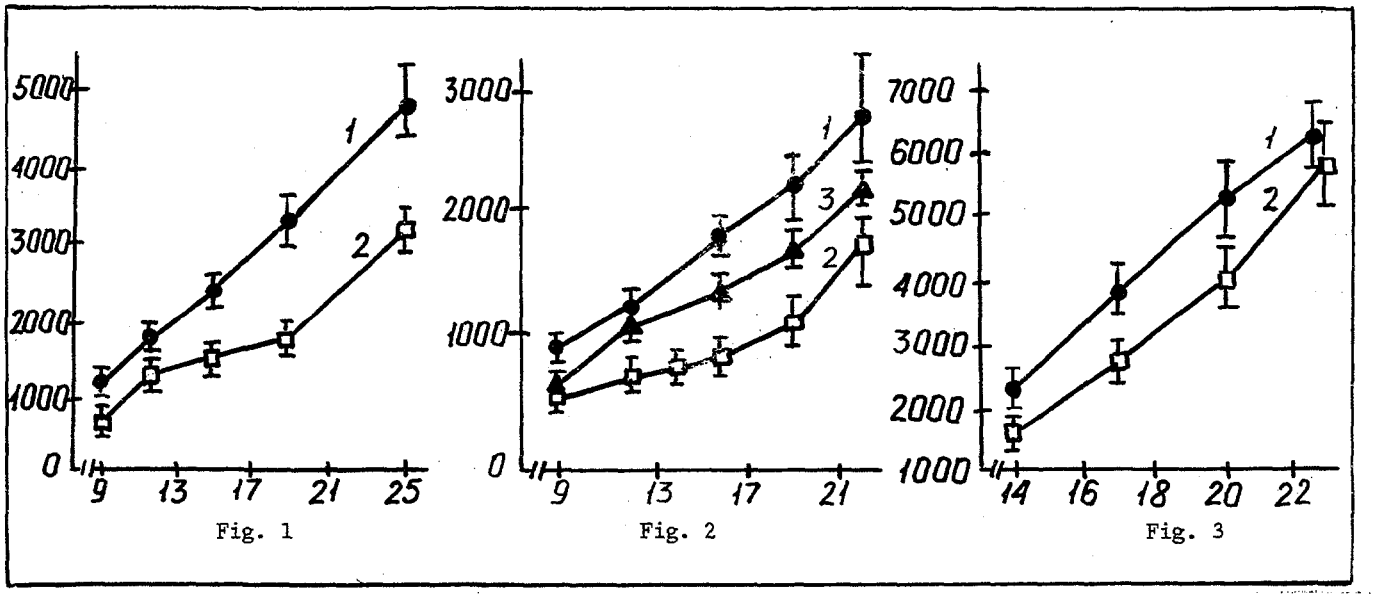

Fig. 1. Effect of biological fluid (BF) C-I on growth of Ehrlich's tumor. Abscissa, time after transplantation of tumor (days); ordinate, volume of tumor (in c.u.). 1) Control animals receiving physiological saline; 2) animals receiving BF C-I.

Fig. 2. Effect of BF C-I and C-II on growth of Ehrlich's tumor. Abscissa, time after transplantation of tumor (in days); ordinate, volume of tumors (in c.u.). 1) Control animals receiving physiological saline; 2) animals receiving BF C-I; 3) animals receiving BF C-II.

Fig 3. Effect of BF C-I on growth of Lewis carcinoma. Abscissa, time after transplantation of tumor (days); ordinate, volume of tumors (in c.u.). 1) Control animals receiving physiological saline; 2) animals receiving BF C-I.

in conventional units (c.u.), was calculated by the formula $V = a \times b \times c$, where a, b, and c are three mutually perpendicular diameters. Each group contained 10 animals The results were subjected to statistical analysis by the Fisher–Student method. Differences were taken to be significant at the $p < 0.05$ level. Values of $M \pm m$ are shown in the graphs.

EXPERIMENTAL RESULTS

The results of the study of the effect of BF C-I on the rate of growth of the ELD tumor from the 9th through the 25th day of observation are given in Fig. 1. During this period significant inhibition of tumor growth was observed in animals receiving BF C-I compared with animals receiving physiological saline.

On the basis of data published by Nelson et al. [5, 6] it can be postulated that humoral factors inhibiting tumor growth are substances with mol. wt. of under 15 kD. The effect of the tumor cell dialysate on growth of Ehrlich's carcinoma was therefore studied. The results of a study of BF C-I and C-II on the rate of growth of the ELD tumor are given in Fig. 2. The volumes of the tumors in animals receiving BF C-I were significantly less from the 9th through the 22nd day of observation than in the control animals receiving physiological saline. Injection of BF C-II also caused significant inhibition of tumor growth on the 9th day of observation compared with the control. However, this inhibitory action was shorter in duration, and on the subsequent days the differences in volume of the tumors in animals receiving BF C-II and physiological saline disappeared. The fact that the actions of BF C-I and BF C-II were not identical can be explained on the grounds that we do not yet know what substances actually mediate activity of BF C-I and C-II, and consequently, as a result of differences in the process of obtaining these fluids, the concentrations of their active substances may not coincide.

The next step was to determine whether BF C-I preserves its inhibitory action on growth of another tumor. Curves showing the kinetics of growth of Lewis carcinoma are given in Fig. 3. On the 14th and 17th days of observation the volumes of the tumors in animals receiving BF C-I were significantly less than in control animals receiving physiological saline ($p = 0.05$). Thus-BF C-I has an inhibitory action not only on the ELD tumor, but also on Lewis carcinoma.

It can be postulated on the basis of these results that ELD tumor cells can secrete certain humoral factors which, when used in accordance with our schedule described above, can inhibit tumor growth. A similar inhibitory action of a larger tumor node on smaller nodes also was observed in clinical practice and, in our opinion, it is a manifestation of concomitant immunity. The creation of an experimental model of this phenomenon will enable the nature of the factors responsible for it to be studied.

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ASCITES FLUID AND TUMOR CELL DIALYSATE AS MODELS OF GROWTH OF EHRLICH'S CARCINOMA AND TERATOMA T-36

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Growth of spontaneous or transplanted tumors evokes an immune response of the affected animals. However, despite the development of an immune response, as a rule the tumor continues to grow [2, 4]. Tumor growth against the background of development of an immune response can evidently be explained by protection of the tumor cells against the host's immune system. It has been shown that protection of this kind can take place with the aid of high-molecular-weight proteins (mol. wt. over 100 kilodaltons) IgG-2 antibodies or antigen-antibody complex [8]. Investigations in vitro also have shown that blood serum of cancer patients and animals with progressively growing tumors specifically inhibits the cytotoxicity of lymphocytes against tumor cells [5-7]. However, the role of tumor humoral factors in the development of a malignant process in the body is difficult to assess, for no suitable techniques have been developed with which to study this phenomenon in vivo.

The aim of this investigation was to study the effect of ascites fluid and cell dialysate of Ehrlich's carcinoma on tumor growth in vivo.

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