CHANGE IN ACTIVITY OF SOME PROTECTIVE REACTIONS OF THE CONNECTIVE TISSUE DURING DEVELOPMENT AND RESOLUTION OF SUBCUTANEOUSLY TRANSPLANTED BROWN-PEARCE CARCINOMA UNDER CONDITIONS OF DECORTICATION AND DIBASOL ACTION

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K. P. Balitskii

Laboratory of Pathogenesis and Pathogenetic Therapy (Supervisor-Candidate of Medical Sciences K. P. Balitskii), Ukraine Institute of Experimental and Clinical Oncology (Director-Academician AN UkSSR R. E. Kavetskii), Kiev
(Presented by Active Member AMN SSSR N. N. Sirotinin)
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The problem of the changes in the reactivity of an organism during progressive carcinogenesis, about the role which the nervous and the connective tissue system plays in this process, is inadequately elucidated in the literature [3-6]. Taking into account the practical importance of investigating the interaction between an organism and a tumor during retrogression of malignant neoplasms, we studied the interrelations between the functional state of the central nervous system, the connective tissue system, and the character of tumor growth.

For the investigations we selected a model of subcutaneously transplanted Brown-Pearce carcinoma. As the observations of A.L. Vorontsova, performed in our laboratory, indicate, Brown-Pearce carcinoma transplanted subcutaneously grows for a certain time and then, usually by the 30-35th day, is spontaneously resolved. This model is valuable in that it affords the opportunity to elicit and study the protective reactions of an organism and to determine the possibility of acting on them not only at the period of progressive carcinogenesis, which leads to death of the animal, but also at the period of spontaneous resolution of the tumor.

EXPERIMENTAL METHOD

The work was carried out on 79 chinchilla rabbits of both sexes weighing 2-2.5 kg. In the I series of experiments (29 rabbits) we investigated the protective reactions of the connective tissue system—carcinolysis, leukocytolysis, phagocytosis—and the character of tumor growth during development and resolution of subcutaneously transplanted Brown-Pearce carcinoma in intact and decorticated rabbits. In the II series of experiments we attempted a nonspecific stimulation of these protective reactions in order to affect the character of tumor growth in the decorticated animals. We have previously described [1, 2] the methods for decortication and determination of the activity of the carcinolytic and leukocytolytic properties of blood serum and the phagocytic capacity of leukocytes. The Brown-Pearce tumor was transplanted on the 11th day after decortication of the rabbits at 2 points on the back by injecting 1 ml of 10% tumor suspension. The activity of the studied reactions and the character of tumor growth were systematically observed for 1-1½ months every 5-6 days beginning with the second or third day after transplantation.

Nonspecific stimulation was accomplished by a subcutaneous injection of dibasol in a dose of 15-20 mg/kg.

Three variants of the experiments were carried out with different conditions for injecting the preparation. In the first variant the preparation was injected daily beginning with the 17th day after transplantation of the tumors until the end of the experiment (during this period spontaneous resolution of the tumor began in the intact animals); in the second variant, daily for 15 days before inoculation of the tumor (an attempt to normalize the protective reactions of the connective tissue system suppressed by decortication before inoculation of the tumor); in the third variant, daily for 15 days before transplantation of the tumor and every three days after it until the end of the experiment.

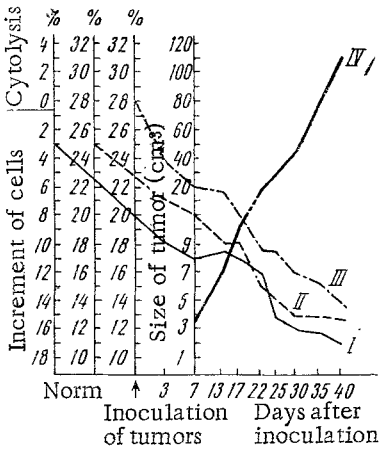

Fig. 1. Change in activity of carcinolysis, leukocytolysis, and phagocytosis in decorticated rabbits during development of subcutaneously transplanted Brown-Pearce tumor. 1, 2, 3) Changes in the activity of the investigated reactions; 4) dynamics of tumor development. Here and in subsequent figures the curves are plotted on the basis of average values obtained after statistical processing.

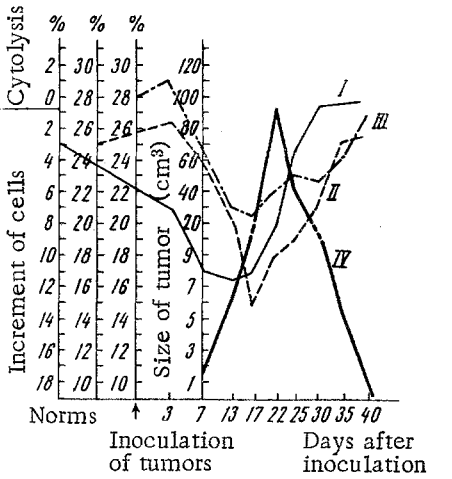

Fig. 2. Change in the activity of carcinolysis, leukocytolysis, and phagocytosis in intact rabbits during the development and resolution of subcutaneously transplanted Brown-Pearce tumor. Designations are the same as in Fig. 1.

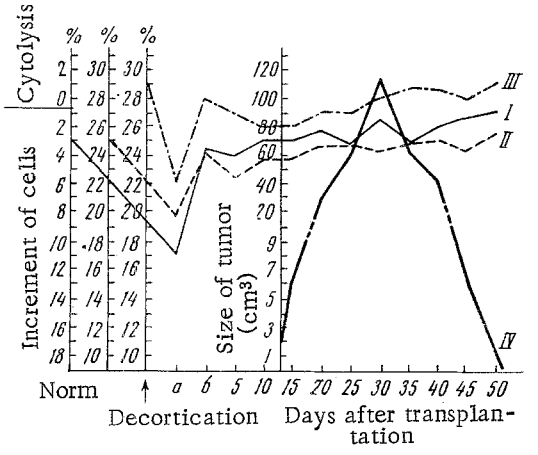

Fig. 3. Variations in the activity of carcinolysis, leukocytolysis, and phagocytosis and the character of the growth of subcutaneously transplanted Brown-Pearce carcinoma in decorticated rabbits with nonspecific stimulation of dibasol. a) Eleventh day after decortications (start of dibasol injection); b) 26th day after decortication (inoculation of tumors, continuation of dibasol injection). Other designations are the same as in Fig. 1.

The results of the experiments were subjected to mathematical processing by the Student-Romanovskii method [7].

EXPERIMENTAL RESULTS

The results of the I series of experiments demonstrated that decortication is accompanied by severe suppression of the investigated protective reactions of the connective tissue system. The tumors reached large size and killed the animals (Fig. 1). The character of tumor growth of the decorticated rabbits differed fundamentally from that of the intact animals, in which the tumors, on reaching a comparatively large size, were resolved by the 35-40th day. In this case, immediately after transplantation we observed in most cases a certain activation of the protective reactions of the connective tissue system and then their profound suppression during progressive growth; the period of resolution of the tumors coincided with the period of complete restoration of the activity of carcinolysis, leukocytolysis, and phagocytosis (Fig. 2).

In the II series of experiments with the first two variants of the injection of dibasol, the attempt to activate the protective reactions of the connective tissue system in the decorticated rabbits and thus to influence the character of tumor growth ended unsuccessfully.

The daily injection of dibasol into the decorticated rabbits prior to transplantation of the tumors and also the continuation of the injection of the preparation after transplantation (third variant of the experiments in this series) stimulated the protective functions of the connective tissue system, which was expressed as a fluctuation in the activity of carcinolysis, leukocytolysis, and phagocytosis at the level observed prior to decortication (Fig. 3). The tumors in this case reached a large size (7×4×3 cm); however by the 40-50th day they were completely resolved.

In the decorticated rabbits that did not received dibasol, the activity of the investigated protective reactions dropped markedly, the tumors reached a large size, and all animals died. Mathematical processing of the results of the experiments showed their statistical reliability.

These investigations give us grounds to assume that one of the causes for the enhancement of the neoplastic process under conditions of decortication is the inhibiting effect of the latter on the protective functions of the connective tissue system. These experiments also indicate the possibility of normalization of the protective reaction of the connective tissue system suppressed by decortication by an appropriate selection of the doses and regimen of injecting dibasol, which in turn induces resolution of subcutaneously transplanted Brown-Pearce tumor in animals. Resolution, as is apparent from these experiments, was never observed in rabbits with the protective functions of the connective tissue system suppressed by decortication.

It is also fitting to note that dibasol stimulation of the nonspecific resistivity of an organism can be carried out even under conditions of decortication.

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