GROWTH OF THE EHRLICH ADENOCARCINOMA WHEN TWO TUMORS ARE TRANSPLANTED SIMULTANEOUSLY OR AT DIFFERENT TIMES INTO VARIOUS REGIONS OF THE ORGANISM

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In a preceding study [2] it was noted that the rate of growth of an Ehrlich carcinoma had a relation to the site of inoculation. It was proven that the adenocarcinoma inoculated into the anterior limb of a mouse grew faster than a similar tumor injected into a posterior limb. At that time there was not demonstrated any regulating factor controlling growth rate of the adenocarcinoma within the limits of one body segment.

The aim of the present study was to observe whether these relationships are preserved when two adenocarcinomas are inoculated into the animal.

EXPERIMENTAL METHODS

300 mice were used – sexually mature females averaging in weight about 20 gm. To produce the subcutaneous tumors, we used, as before, a suspension of the Ehrlich adenocarcinoma (0.2 ml with each injection). In some of the experiments the two tumors were injected simultaneously into different regions of the body, the weight of the tumors being determined when the animals were sacrificed on the 15th day. In some of the other experiments the interval between the two inoculations consisted of 10 days, the animals being sacrificed 10 days after the second inoculation. In each series there was a control group which received only the one inoculation into the corresponding portion of the body. When comparing the rate of growth for the tumors, the probabilities for their attaining a given size were calculated mathematically from the average of their weights P [4].

EXPERIMENTAL RESULTS

Figure 1 presents the data on the average weights of the tumors inoculated simultaneously into different body regions of the mouse, the number of animals used in each group being indicated within the parentheses.

Analysis of the figure indicates that simultaneous inoculation of two Ehrlich adenocarcinomas results in the one inoculated into the region of the fore limb outgrowing the one inoculated into the region of the hind limb on the same side ($p = 0.021$). Within the limits of the one body segment there is no difference in the rate of growth for the two simultaneously inoculated tumors ($p = 0.368$ and $p = 0.484$).

Figure 2 presents the averages for the tumors simultaneously inoculated into the fore limb on one side and the hind limb on the other. In this situation, also, the tumor on the fore limb grows more rapidly than the one in the hind limb (in control, $p < 0.0001$; in experiment, $p = 0.0001$). The general rate of growth is much greater here than in the preceding series. At the same time, simultaneous inoculation of the two tumors never caused the average tumor weights to decrease when compared with the controls.

Thus it can be seen that the peculiarities in the growth of Ehrlich adenocarcinomas arising from the region

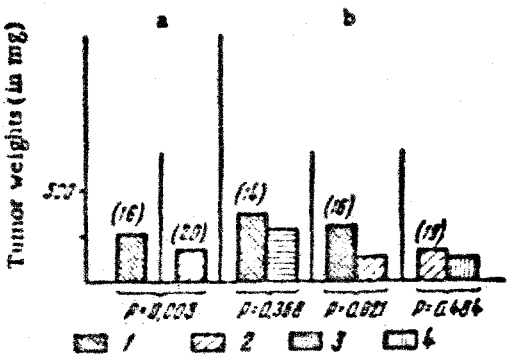

Fig. 1. Growth of Ehrlich adenocarcinoma in the region of the fore limbs and hind limbs on the same side of the body when the inoculations were made simultaneously and the animals were sacrificed 15 days after the inoculations. a) experiment; b) control; 1) right fore limb; 2) right hind limb; 3) left fore limb; 4) left hind. Within parentheses is indicated the number of animals.

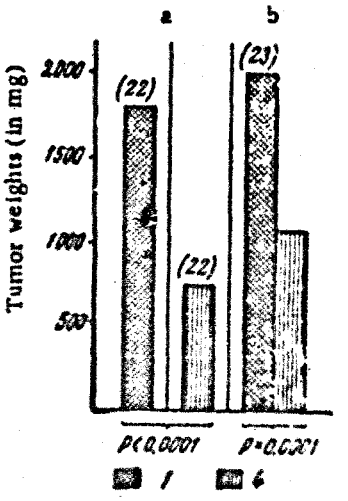

Fig. 2. Growth of Ehrlich adenocarcinoma simultaneously injected into the region of one fore limb and the region of the hind limb on the opposite side, the animals being sacrificed 15 days after inoculation. Labelling as in Figure 1.

of the inoculation sites manifest themselves also when two tumors are inoculated into the animal simultaneously

In Figure 3 are shown the average tumor weights of 20-day growths injected into the right fore and hind limb regions. The experimental animals received, 10 days after the first inoculation, a second tumor inoculation in the region of the other limb of the same side.

There was no significant difference in the rate of growth on the part of the first inoculated tumors ($p = 0.368$). At the same time, in the control animals, the average weight of the tumors in the anterior regions was greater than in the posterior ($p = 0.0004$).

When there was inoculated an adenocarcinoma into animals already having a 20 day tumor, there did not develop a difference in the growth of 10 day tumors when those in the region of the fore limb were compared with those in the region of the hind limb, neither in the experiment ($p = 0.424$) nor in the control ($p = 0.134$). It was not clear why the control animals failed to show a difference.

This does seem to show, however, that, when two Ehrlich adenocarcinomas are inoculated into the same animal at different times, the peculiarities in the rates of growth previously noted were no longer present.

The average weight of the 10-day tumors in the control groups exceeded the weight of the similar carcinomas inoculated into corresponding areas into animals already having tumors ($p = 0.0001$ and 0.021).

This seems to indicate that the presence of a previous tumor gives a certain degree of immunity to a repeated inoculation with the same tumor.

In one case, there were no differences (see Fig. 3). In the growth of the 20-day tumors and the controls ($p = 0.23$). In another instance the average weight of the 20 day tumors in the controls exceeded the weights in the corresponding group ($p = 0.0003$). This last speaks against the prevailing view that the organism develops resistance as the secondary tumors develop, not interfering with the growth of the original inoculations [1].

It is possible that we should seek in this the reason for the fact that there is no difference in the rate of growth of the 20 day tumors as far as the tumors in the anterior and posterior limb regions are concerned.

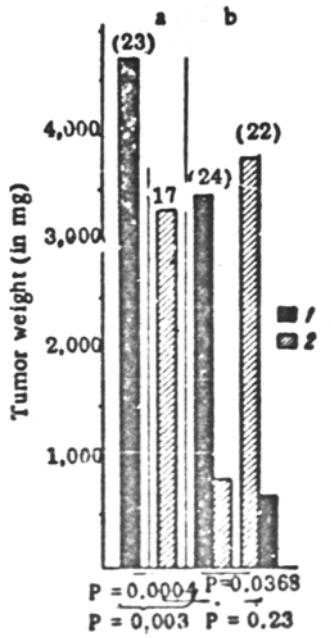

Fig. 3. Growth of Ehrlich adenocarcinoma in the fore and hind limb regions on the 20th day when there is already present a 10-day tumor. Labelling as in Fig. 1.

The underlying reasons for the uneven rates of adenocarcinoma growth depending on the sites of inoculation have not been analyzed so far. We have shown in the present study that secondary inoculation upsets this differential. This second inoculation can be regarded as an additional stimulant [3] which, with the aid of certain reflex mechanisms, upsets the rate of growth for the first tumor inoculated, altering the resistance in the focus of its development. However, we cannot talk with assurance about the nature of these reflex mechanisms altering the organism resistance by virtue of the second tumor having been inoculated, until after additional studies have been made, namely, inoculating the secondary irritant (second tumor) into various regions of the body.

As long as we do not possess this additional data, we can only draw attention to the single fact that secondary inoculation of the adenocarcinoma causes such immunological changes within the organism that the growth differentials previously noted are no longer present.

SUMMARY

When two Ehrlich adenocarcinomas were transplanted simultaneously, the anterior one grew more intensely. When there was time interval between the two inoculations, this difference disappeared, probably as a result of immunological alterations arising in the organism.

LITERATURE CITED

[1] F. M. Bricker and L. I. Timofeeva, in book: Antitumor Immunity,* pp. 9-19 (1939).

[2] O. I. Epifanova, Byull. Eksptl. Biol. i Med., 1956, No. 11, pp. 55-57.

[3] S. I. Lebedinskaya and A. A. Soloviev, Klin. med., 1951, Vol. 29, No. 3, pp. 11-15.

[4] V. I. Romanovsky, Use of Mathematics in Statistical Evaluation of Experimental Data,* Moscow–Leningrad (1947).

* In Russian.