ACCELERATION OF TRANSPLANTED TUMOR GROWTH IN APPENDECTOMIZED RATS

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Progress in immunology has greatly broadened our ideas on the character and mechanisms of the influence both of the immune system as a whole and of its individual components on tumor growth. However, with regard to the appendix, whose lymphoid tissue is unique in its structure and function [7, 9-11], this problem has not been adequately studied. Investigation of correlation between the frequency of onset tumors and removal of the appendix in man has not yet led to the discovery of any definite general rules [6, 8]. The writers have tried to discover such correlation under experimental conditions. This paper gives the macroscopic data of these experiments, to supplement the morphological observations which were published previously [4].

EXPERIMENTAL METHOD

Inbred Wistar and noninbred albino rats were used. Appendectomy was performed under sterile conditions 2-3 weeks before transplantation of the tumor. Laparotomy only was performed on animals of the control group. The operations were performed under ether anesthesia. A carcinoma RS-1 (a strain of spontaneously arising hepatocholangial adenocarcinoma) was transplanted subcutaneously on the side opposite to the operation wound. The tumor was injected in the form of a cell suspension in a dose of 0.5 ml in medium 199 in the ratio of 1:3 and 1:5. The day of transplantation of the tumor was counted as the beginning of the experiment. In two experiments, retinoids were injected into the animals as nonspecific stimulators of immunity [2, 5]. A 1.5% oil solution of retinoid C_{15}-trans-ester and a 1% oily solution of all-transmethylretinoate were used for this purpose. Both substances were obtained from the

TABLE 1. Effect of Appendectomy on TSI in Male Wistar Rats with Transplanted Carcinoma RS-1 (27th day of experiment, M ± m)

Group of animals	Experimental conditions	Number of animals studied	Weight of animals with tumor, g	Weight of tumor, g	TSI
1	Carcinoma RS-1 + appendectomy	8	109,0±3,5	3,4±0,4	3,1±0,4
2	Carcinoma RS-1 + laparotomy	10	106,0±1,9	1,6±0,35	1,4±0,3
3	Carcinoma RS-1	12	174,4±4,0	1,3±0,3	1,1±0,2

Legend. $P < 0.001$ — significance of differences between results in groups 1 and 2.

TABLE 2. Effect of Appendectomy on TSI in Noninbred Male Rats with Transplanted Carcinoma RS-1 (23rd day of experiment, M ± m)

Group of animals	Experimental conditions	Number of animals studied	Weight of animals with tumor, g	Weight of tumor, g	TSI
1	Carcinoma RS-1 + appendectomy	10	120,5±4,4	9,3±0.7	8,4±0.8
2	Carcinoma RS-1 + laparotomy	6	132,0±5,9	7,2±0,8	5,1±0,4
3	Carcinoma RS-1	6	146,2±10,2	5,3±0,6	3,9±0,4

Legend. $P < 0.001$ — significance of differences between results in groups 1 and 2.

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TABLE 3. Effect of Appendectomy on TSI in Old Male Wistar Rats with Transplanted Carcinoma RS-1 (35th day of experiment, M ± m)

Group of animals	Experimental conditions	Number of animals studied	Weight of animals with tumor, g	Weight of tumor, g	TSI
1	Carcinoma RS-1 + appendectomy	13	232,0±9,6	13,2±1.9	5,1±0,9
2	Carcinoma RS-1 + laparotomy	10	230,0±5,9	11,0±1.2	6,1±0,6
3	Carcinoma RS-1	6	250,0±12,4	14,9±3.2	6,4±1,4

Legend. $P < 0.001$ — a significance of differences between results in groups 1 and 2.

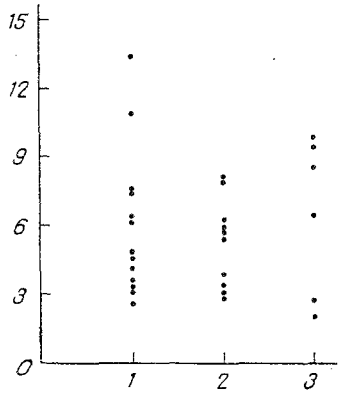

Fig. 1. Effect of appendectomy on TSI in old Wistar male rats with transplanted carcinoma RS-1 (35th day of experiment, scatter diagram). Abscissa: 1) carcinoma RS-1 + appendectomy; 2) carcinoma RS-1 + laparotomy; 3) carcinoma RS-1; ordinate, TSI (in %).

TABLE 4. Effect of 1% All-Transmethylretinoate on Growth of Carcinoma RS-1 in Appendectomized Female Wistar Rats (30th day of experiments, M ± m)

Group of animals	Experimental conditions	Number of animals studied	Weight of animals with tumor, g	Weight of tumor, g	TSI
1	Carcinoma RS-1 + methylretinoate + appendectomy	8	159,0±7,3	4,8±0,57	3,1±0,4
2	Carcinoma RS-1 + methylretinoate + laparotomy	10	171,4±7,0	3,5±0,38	2,0±0,2
3	Carcinoma RS-1 + methylretinoate	20	183,0±4,8	3,1±0,37	1,7±0,2

Legend. Each animal received 20 mg of retinoid. $P < 0.001$ — significance of differences between results in group 1 and 2.

TABLE 5. Effect of 1.5% Trans-Ester of C_{15}-Retinoic Acid on Growth of Carcinoma RS-1 in Appendectomized Female Wistar Rats (27th day of experiments, M ± m)

Group of animals	Experimental conditions	Number of animals studied	Weight of animals with tumor, g	Weight of tumor, g	TSI
1	Carcinoma RS-1 + retinoid C_{15} + appendectomy	8	133,5±8,2	4,0±0,33	3,1±0,3
2	Carcinoma RS-1 + retinoid C_{15} + laparotomy	7	111,4±4,8	1,6±0,2	1,5±0,2
3	Carcinoma RS-1 + retinoid C_{15}	8	143,6±4,6	1,5±0,27	1,1±0,2

Legend. Each animal received 7.5 mg of retinoid. $P < 0.001$ — significance of differences between results in groups 1 and 2.

Laboratory of Chemistry of Polyene Compounds (Head, Professor G. I. Samokhvalov), "Vitaminy" Research and Production Combine, Ministry of the Medical Industry of the USSR. The first compound was injected as a single dose of 0.5 ml subcutaneously, contralaterally to the tumor, weekly for 30 days. At the end of the experiments the rats were killed under ether anesthesia. Animals with a tumor and the tumors after removal were weighed. A tumor-somatic index (TSI) was determined, in percent, as the ratio between these two values in each animal. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The experiments showed that appendectomy accelerates growth of carcinoma RS-1 in young animals. This was shown as an increase both in the absolute (weight of the tumor) and relative (TSI) indices. It must be pointed out that commensurate results, as regards the magnitude of error also, were obtained both in inbred rats and in genetically heterogeneous noninbred animals (Table 1 and 2). This phenomenon is evidently based on the defect of immune protection developing as a result of removal of some of the lymphoid tissue. This hypothesis was confirmed by the results of experiments on old animals (weighing 250 ± 12 g), in which age involution of the lymphoid system had developed, and experiments in which adjuvant stimulation of immune defense was used. Appendectomy in the old animals did not change the rate of growth of the tumor, which remained comparatively high; this will be clear from analysis of the mean values and ranges of variation of weight of the tumors in the control and experimental animals (Table 3; Fig. 1). Stimulation of immune antitumor defense by retinoids, which proved effective according to data obtained by other workers [1, 3], did not render the host animal more capable of restraining tumor growth (Tables 4 and 5). The suggestion that lymph nodes of the appendix are involved in the restraint of tumor growth is supported by changes observed in the organs of immunogenesis in appendectomized animals affected with tumors [4].

The transplanted tumor thus grew more rapidly in rats after appendectomy. This effect was manifested in young inbred and noninbred animals, was not abolished by adjuvants, and did not develop in old rats.

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