EFFECT OF SPLENECTOMY ON GROWTH OF SYNGENEIC TRANSPLANTED SARCOMAS IN MICE

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The effect of splenectomy on growth of syngeneic sarcoma A-3174 was studied in (CBA × C57B1/6)F_1 hybrid mice. Removal of the spleen 1-2 h or 10 days before and also 3 days after inoculation of the tumor cells gives rise to definite inhibition of the natural immunity of the recipients to growth of the syngeneic tumor, manifested in particular by the earlier death of the animals. Earlier appearance of the tumor was observed only after splenectomy performed 1-2 h before or 3 days after inoculation of the tumor cells. Splenectomy carried out 10 days after injection of the tumor cells did not affect growth of the tumor.

Animals with tumors as a rule develop splenomegaly [4, 7, 11, 12]. Investigations have been undertaken to study the evident effect of splenectomy on tumor growth [1, 3, 5, 6, 8, 10]. Old and co-workers [8], for instance, observed increased resistance of splenectomized mice to nonspecific sarcoma S-180, whereas Bard and Pilch [3] found no effect of splenectomy on growth of a primary chemically induced sarcoma C3H of mice. In Khaletskaya's experiments [1] splenectomy led to increased resistance of the animals to tumor development. In these investigations splenectomy was carried out usually before inoculation of the tumor.

The object of the present investigation was to study the role of lymphoid tissue in antitumor immunity, using splenectomy performed at various times before and after inoculation of the tumor for this purpose.

EXPERIMENTAL METHOD

(CBA × C57B1/6)F_1 hybrid mice weighing 19-23 g were used as recipients of the tumor, with 10 animals in each group. Sarcoma A-3174, a strain obtained in the writer's laboratory in one of ten females after two sessions of x-ray irradiation of (CBA × C57B1/6)F_1 hybrids, was used for the experiments. The strain took successfully in 100% of cases in the original line. The dose of tumor cells received after trypsinization and inoculated subcutaneously into the right flank was 10^5. The viability of the cells was determined by staining with 0.5% eosin solution. Splenectomy and the corresponding mock operation were performed 10 days before, 1-2 h after, and 3 and 10 days after inoculation of the tumor cells.

EXPERIMENTAL RESULTS

It will be clear from Table 1, which gives the conditions and results of nine experiments, that splenectomy performed 1-2 h before inoculation of the tumor cells caused a much earlier appearance of the tumor, more rapid death of the tumor-bearing mice, but at the same time a decrease in the weight of the tumor ($P < 0.01$) than the control. Splenectomy performed 10 days before injection of the tumor cells also led to earlier death of the recipients ($P < 0.01$) and to a decrease in the weight of the tumor ($P < 0.05$), but did not affect the time of its appearance.

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TABLE 1. Effect of Splenectomy on Growth of Sygeneic Sarcoma in (CBA × C57Bl/6)F_1 Mice. Dose of Tumor Cells Inoculated 10^5

Group No.	Interval between operation and inoculation of tumor (in days)		Mean time of appearance of tumor (in days)			Mean period of survival (in days)			Mean weight of tumor (in g)		
	splenectomy	laparotomy	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2
1	10+	—	10,9±0,11	>0,05	>0,05	22,1±1,34	<0,01	<0,01	7,1±0,28	<0,05	<0,05
2	—	10+	11,2±0,41	>0,05	—	32,6±0,9	>0,05	—	10,0±0,91	>0,05	—
3	—	—	11 ±0,67	—	—	33,3±1,57	—	—	10,35±1,1	—	—
4*	1—2+	—	7,1±0,34	<0,01	<0,01	25,1±1,11	<0,01	<0,01	6,66±0,56	<0,01	<0,01
5*	—	1—2+	10,0±0,45	>0,05	—	34,6±1,23	>0,05	—	10,11±0,5	>0,05	—
6	3—	—	7,5±0,34	<0,01	<0,01	26,9±0,68	<0,01	<0,01	8,5± 1,23	>0,05	>0,05
7	—	3—	10,5±0,62	>0,05	—	32,5± 1,1	>0,05	—	11,1± 1,04	>0,05	—
8	10—	—	12 ±0,22	>0,05	>0,05	30 ± 1,11	>0,05	>0,05	8,5± 1,17	>0,05	>0,05
9	—	10—	11,5±0,7	>0,05	—	32,7± 1,4	>0,05	—	10,3± 0,8	>0,05	—

* Interval in groups 4 and 5 measured in hours.

Legend: the signs + and - shown after the figures mean that the operation was carried out the corresponding period before or after inoculation of the tumor cells. P_1) Significance of difference for comparison between splenectomized or laparotomized and intact animals; P_2) significance of difference for animals undergoing splenectomy and laparotomy.

Splenectomy 3 days after inoculation of the tumor cells caused the earlier appearance of a tumor than in the control and the more rapid death of the recipients ($P < 0.01$). Splenectomy performed 10 days after injection of the tumor cells had no effect on growth of the tumor. In this case when the spleen was removed it was found to be definitely enlarged ($P < 0.01$). Laparotomy did not affect the growth of the tumor.

Removal of the spleen 1-2 h or 10 days before, and also 3 days after inoculation of the tumor cells thus caused definite inhibition of the natural immunity of the recipient to growth of the syngeneic tumor, as shown by the more rapid death of the animals. A marked decrease in weight of the tumor was observed when splenectomy was performed 1-2 h or 10 days before injection of the tumor cells. Earlier appearance of the tumor was observed only after splenectomy performed 1-2 h before or 3 days after inoculation of the tumor cells.

Consequently, a marked decrease in the content of lymphoid tissue in the body as a result of splenectomy led to a decrease in natural antitumor immunity, and this was particularly marked if splenectomy was performed 1-2 h before and 3 days after inoculation of the tumor. A less marked decrease in immunity was observed if the tumor cells were injected 10 days after splenectomy, possibly on account of the compensatory regeneration of the lymphoid tissue which had occurred at this time [2].

The results of these experiments suggest that during the first few days after inoculation of tumor cells there is a certain stage in which the immune system is sensitive to removal of the spleen. It is in this first (sensitive to splenectomy) stage that definite relations are established between the recipient's immune system and the tumor cells injected. In the later period (10 days after inoculation of the tumor cells) splenectomy does not affect growth of the tumor. Evidently if a sufficiently long time for accumulation of a certain threshold number of tumor cells elapsed after inoculation of the tumor, the depression of natural immunity caused by splenectomy does not affect growth of the tumor.

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