EFFECT OF TUBERCULOUS INFLAMMATORY PROCESS IN THE LUNGS ON RESISTANCE TO TUMORS

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Tumors were induced in rats with 20-methylcholanthrene. Preliminary (11-13 days beforehand) injection of Mycobacterium tuberculosis cells in an oil–water emulsion into the lung tissue reduced the resistance of the animals to tumors. It is postulated that this effect is due to intensification of autoimmune processes as a result of injection of the mycobacteria.

KEY WORDS: tumors; mycobacteria.

The writer previously discovered a decrease in the resistance of rats to chemically induced tumors following injection of Freund's complete adjuvant (FCA) subcutaneously into the footpad 10-12 days before administration of the carcinogen [1]. The active antigenic principle of stimulators of the FCA type is known to be killed cells of Mycobacterium tuberculosis or their complete antigens.

The object of this investigation was to study the effect of an inflammatory process produced in the lungs by both killed and living cells of Mycobacterium tuberculosis on the resistance of experimental animals to tumors.

EXPERIMENTAL METHOD

The experiments consisted of three series. Series I was carried out on male Wistar rats (11 control and 14 experimental) and series II on 72 noninbred male (35) and female (39) rats. The experimental animals of series II were divided into three groups (29, 12, and 31 animals), so constituted that the ratio of males to females was about the same in each group. The experiments of series III were carried out on female Wistar rats (29 experimental and 22 control). The control rats in each series received no treatment other than injection of the carcinogen. An inflammatory focus was produced in the lungs by injection of M. tuberculosis cells in the experimental rats of series I 12 days, of series II 13 days, and of series III 11 days before administration of the carcinogen. For this purpose the animals of the experimental groups in each series received an injection of 0.04 ml of a suspension of BCG in a concentration of 1 mg to 0.1 ml of a 50% oil–water emulsion. In the first two series of experiments killed mycobacteria were used, whereas in series III the organisms were living. The rats of group 2 of series II received an injection of the oil–water emulsion without mycobacteria, in the same dose and by the same method.

The carcinogen used in all series of experiments was 20-methylcholanthrene. The compound was injected intramuscularly in a dose of 3 mg in 0.3 ml apricot oil into the thigh.

EXPERIMENTAL RESULTS

The general condition of the rats receiving injections of M. tuberculosis cells did not differ appreciably from that of the control animals. In the experiments of series I, after 99 days tumors appeared in one of 11 control rats and in four of 14 experimental rats; after 134 days tumors had appeared in 3 of the control animals and 10 of the experimental animals. At the time of sacrifice, 165 days after injection of the carcinogen, tumors were observed in 10 rats of the control group and in all 14 rats of the experimental

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TABLE 1.

Series	Group	Preliminary treatment		Number of rats in group	Number of rats with tumors at different times of observation after injection of carcinogen					
					86 days	104 days	134 days	155 days	171 days	200 days
II	1	Control		22	—	1	8	13	16	20
			P		>0,1	>0,05	<0,001	<0,001	<0,01	>0,2
	2	Oil–water emulsion		12	—	—	3	6	7	12
			P		>0,1	<0,05	<0,001	<0,001	<0,01	1,0
	3	Mycobacteria in oil–water emulsion		23	3	5	19	22	23	23
					96 days	108 days	123 days	142 days	158 days	178 days
III	1	Control		22	—	2	5	7	12	15
			P		<0,001	<0,001	<0,001		<0,001	<0,001
	2	Mycobacteria in oil–water emulsion		29	12	13	21	25	28	29

Note. Significance of differences calculated relative to group of animals treated with FCA.

groups. Differences in the number of tumors appearing in the experimental and control groups after 134 days were statistically significant ($P < 0.05$).

In their histological structure the tumors in both the experimental and the control groups were spindle-cell and polymorphocellular sarcomas.

Data on the development of tumors in the animals in the experiments of series II are given in Table 1. Clearly the most intensive tumor development occurred, just as in the experiment described above, in animals with a focus of tuberculosis inflammation in the lungs. In rats receiving an injection of oil–water emulsion into the lung tissues (second control group) the intensity of tumor development did not differ significantly from that in the first control group.

Information on the dynamics of appearance of tumors in the control and experimental rats in the experiments of series III (injection of living mycobacteria) is also given in Table 1. It shows that there was a marked decrease in resistance to tumor development in the experimental animals of this series also.

Either very slight scar changes or foci of encapsulated debris were present in the lung tissue at the site of injection of FCA in the experimental rats of all series.

A focus of tuberculous inflammation in the lungs under the experimental conditions used thus had a stimulating effect on carcinogenesis. The following explanation of these results can be suggested. Pathological changes in the tissues are known to cause the appearance of autoantibodies against them. It is also known that strong autoimmune reactions can arise after injection of tissue homogenates from individuals of the same species mixed with FCA into animals [4-8]. The writer has shown that an increase in the content of precipitating autoantibodies takes place in the early stages of the reaction to injection of FCA alone into the footpad [2]. An increase in the content of autoantibodies under these circumstances also was observed during the action of a carcinogen. According to data in the literature, when pathological changes caused by M. tuberculosis are present in the lungs the titer of autoantibodies is particularly high [3]. Conditions for autoimmune reactions are also created by injection of mycobacteria suspended in oil and water into the lung. This suggests that during exposure to these factors or to immune processes play an important role in the mechanisms of the decreased resistance of the body to tumor development.

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