EFFECT OF SUBLETHAL PREIRRADIATION OF RECIPIENTS ON GROWTH OF GRAFTED SYNGENEIC TUMORS IN NEWBORN MICE

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UDC 616-006-089.843-089.163:
615.849.1]-092.9

KEY WORDS: newborn mice; hepatoma; ovarian carcinoma; irradiation.

The great importance of immunologic factors has been demonstrated by studies of the mechanisms of pathogenesis of various tumors [2]. Immunologic insufficiency as a rule leads to stimulation of tumor growth *in vivo*. However, a few years ago it was shown in the writer's laboratory that some tumors grow less well when transplanted into syngeneic newborn mice than into mature mice. Of 12 tumor strains studied, eight strains grew less well in newborn mice under certain conditions. These included both tumors arising spontaneously and subsequently transplanted a few times and also continuous strains [11, 12].

The causes of inhibition of growth of certain tumors in newborn mice are not clear. The object of the investigation described below was accordingly to study the possible role of the immunologic system, using the method of total sublethal preirradiation of the recipients before grafting.

EXPERIMENTAL METHOD

Experiments were carried out on (CBA × C57BL/6j)F_1 mice aged 1 day and 8-12 weeks, bred at the "Stolbovaya" nursery of the Academy of Medical Sciences of the USSR. Ovarian carcinoma OC-1-72 and hepatoma H-2-73 were maintained by subcutaneous passage through (CBA × C57BL/6j)F_1 males. As a rule these tumors grow more slowly in newborn animals than in adults [11].

The recipients were inoculated with 0.1 ml of a suspension of single tumor cells in medium No. 199, obtained by treatment with trypsin [13], or of a coarse suspension obtained by means of a metallic mincer, subcutaneously in the spinal region. The coarse suspension was injected through a needle from a blood-taking system (Industrial Enterprise Board, All-Union Rehabilitation Center for the Deaf and Dumb) and the wound was quickly sealed with BF-6 glue. This procedure prevented escape of the injected material. The newborn mice were replaced with their mothers after the glue had dried completely. Some mice were subjected to a single session of whole-body irradiation in a sublethal dose on the "Stebel'" apparatus 1 h before injection of the tumor. A ^{137}Cs source was used and the mean dose rate was 900 rads/min. Newborn mice were irradiated in a dose of 750 rads and adults in a dose of 600 rads. The mice were killed on the 9th-10th day after transplantation, the tumors were removed and freed from nontumor tissues, and weighed. The results were processed by calculating the arithmetic mean and standard error ($M \pm m$). The significance of differences between means was determined by Student's t-test at the $P \leqslant 0.05$ level. Altogether six experiments were carried out with the ovarian carcinoma and seven with the hepatoma on 299 newborn and 233 adult mice.

EXPERIMENTAL RESULTS

Since consistent results were obtained in all the experiments, the results for four of the 13 experiments are given in Table 1. The OC-1-72 tumor developed least successfully of all in the irradiated newborn mice (two of the six experiments of this series are illustrated in Table 1). However, the difference in the mean weight of the tumors in irradiated and nonirradiated newborn mice was not significant in three of the six experiments. The difference between the weight of the tumors in the groups of irradiated newborn and nonirradiated adult mice was significant in four of the six experiments, but between the groups of nonirradiated

Laboratory of Experimental Immunotherapy of Tumors, Oncologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR L. M. Shabad.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 2, pp. 195-197, February, 1981. Original article submitted July 18, 1980.

 0007-4888/81/9102-0184$07.50

TABLE 1. Effect of Sublethal Preirradiation of Recipients on Growth of Grafted Tumors in Syngeneic Newborn Mice

Expt. No.	Group No.	Mice	No. of mice	Weight of tumor, g (M±m)	P
		Newborn			
	1	irradiated	12	0,06±0,01	$P_{2-4}>0,05$
1	2	nonirradiated	8	0,23±0,03	$P_{1-4}<0,001$
		Adult			
	3	irradiated	13	0,31±0,03	$P_{1-2}<0,001$
	4	nonirradiated	12	0,33±0,03	$P_{3-4}>0,05$
		Newborn			
	1	irradiated	10	0,08±0,01	$P_{2-4}<0,001$
2	2	nonirradiated	9	0,13±0,02	$P_{1-4}<0,001$
		Adult			
	3	irradiated	11	0,51±0,04	$P_{1-2}>0,05$
	4	nonirradiated	12	0,48±0,04	$P_{3-4}>0,05$
		Newborn			
	1	irradiated	12	0,22±0,03	$P_{2-4}<0,001$
3	2	nonirradiated	23	0,75±0,04	$P_{1-4}<0,001$
		Adult			
	3	irradiated	10	1,38±0,11	$P_{1-2}<0,001$
	4	nonirradiated	10	2,88±0,24	$P_{3-4}<0,001$
		Newborn			
	1	irradiated	16	0,23±0,03	$P_{2-4}<0,001$
4	2	nonirradiated	6	0,29±0,02	$P_{1-4}<0,001$
		Adult			
	3	irradiated	10	1,38±0,18	$P_{1-2}>0,05$
	4	nonirradiated	10	2,10±0,34	$P_{3-4}>0,05$

Legend. Female (CBA × C57BL/6j)F_1 mice were used in experiments 1 and 3, males in experiments 2 and 4. Mice in experiments 1 and 2 were inoculated subcutaneously with ovarian carcinoma in a dose of 0.1 ml of a coarse suspension diluted with medium No. 199 (1:2 w/v), in experiments 3 and 4 with hepatoma in a dose of 0.1 ml of suspension (1:3 w/v). Tumors OC-1-72 at the 13th, 14th, and 15th passages and tumors H-2-73 at the sixth, seventh, and eight passages were used in the experiments.

newborn and adult recipients it was significant in only two of the six experiments. In three experiments significant inhibition of tumor development compared with nonirradiated adults was observed only in irradiated newborn recipients. Irradiation of adult mice, which was done in two experiments, did not affect tumor growth.

Tumor H-2-73 also developed most slowly of all in irradiated newborn mice (two of the seven experiments of this series are shown in Table 1). Inhibition of growth of this tumor in the irradiated newborn mice was significant compared with nonirradiated adult mice in all seven experiments and in the nonirradiated newborn mice compared with nonirradiated adults in five of the seven experiments. Only in three of the seven experiments did tumor H-2-73 grow significantly more slowly in the irradiated adults than in nonirradiated adult recipients. In the remaining four experiments the rate of growth was the same.

Irradiation of newborn mice before transplantation of the tumor thus intensified the phenomenon of inhibition of tumor growth. Preirradiation of adult recipients in sublethal doses is frequently used to suppress their immunocompetence. It has been shown that irradiation stimulates growth of certain tumors [4, 10] and inhibits growth of others [5]. Different subpopulations of the recipient's immunocompetent cells, participating in the regulation of tumor growth, differ in their sensitivity to irradiation. It has recently been suggested that a possible cause of inhibition of tumor growth in irradiated recipients is depression of activity of radiosensitive T suppressors [3]. T-suppressor activity is known to be high in newborn animals [8] and irradiation can depress it [7]. It is possible, therefore, that the inhibition

of tumor growth in newborn mice by irradiation discovered in the present investigation is connected with the disturbance of T-suppressor function. However, it must be remembered that irradiation can also affect tumor growth by its action on nonimmunologic factors of the recipient. According to available data [6, 9], the acceleration of growth of weakly immunogenic tumors is unconnected with inhibition of immunocompetence of the recipients by sublethal irradiation. The authors cited attach great importance to the action of irradiation as a stress factor. Inhibition of growth of certain syngeneic and allogeneic tumors caused by preirradiation may be connected with inhibition of the connective tissue response to transplantation of the tumor which facilitates its survival and growth [1].

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IMMUNOFLUORESCENCE STUDY OF CHANGES IN THYMUS MYOID CELLS IN PATIENTS WITH MYASTHENIA

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UDC 616.74-009.54+616.831.8-009.18]-07

KEY WORDS: thymus; myoid cells; myasthenia gravis; autoimmune diseases.

Antibodies against antigens of thymus myoid cells common with antigens of muscle tissue are known to be present in high titer in the blood of patients with myasthenia gravis [2, 3, 9]. On the basis of these findings it has been suggested that such antibodies are evidently among the possible pathogenetic factors in this disease, for by injuring the myoid cells of the thymus under certain conditions they can lead to the development of an autoimmune thymitis, which is characteristic of several autoimmune diseases, including myasthenia [10]. Besides the formation of autoantibodies against antigens of myoid cells, other important evidence of damage to these thymus cells is demonstration of their immunomorphological changes in the thymus of patients with myasthenia.

This paper describes a comparative study, by the immunofluorescence method, of myoid cells in normal subjects and myasthenia patients with the aim of discovering possible changes in this heterologous tissue of the thymus in this disease.

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(Presented by Academician of the Academy of Medical Sciences of the USSR P. A. Vershilova.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 2, pp. 197-199, February, 1981. Original article submitted March 28, 1980.

0007-4888/81/9102-0186$07.50