Abscopal Effect and Recovery of Splenic Weights of Mice

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遠隔作用とマウス脾臓重量の回復

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X線の全身または部分照射によるマウスの脾臓重量の経時的変化について研究を行なつた．500Rの全身照射の場合には照射後9日目に脾臓重量の回復が見られた．1,000Rの胸腹部照射の場合には照射後7日目に回復が見られた．遠隔作用を見るために胸腹部1,000R照射後に直ちに下肢部に種々の線量を与えた群について，照射後の脾臓重量の変化を観察した．胸腹部と下肢部の照射を受けた群では7日目までは下肢部の照射の影響が殆んど見られなかつた．これらの群の大部分は約11日目に最高の重量を示し，14日目には再びわずかの減少を見た．下肢部照射の線量依存性は11日目には著明で700Rまでは線量の大きい程重量も大きくなつた．すなわち下肢部からの遠隔作用は7日目までは見られないが，11日目の回復期にその作用が観察された．

Introduction

The loss of weight of the spleen after irradiation has been shown to be a sensitive indicator and has been used as an indicator for RBE.[11] The present experiments were designed to establish an effect on weight of irradiated spleen by irradiation of lower body with graded doses. Mole[8] has proposed the use of terms "abscopal" to indicate effects produced in one tissue by irradiation of another, thus avoiding the use of the term "indirect" which has another meaning in radiation biology at the molecular level. Raventos[9] has shown that irradiation of the spleen alone resulted in spleen weight losses independent of X-ray dosage over the range 300 to 750 R. The irradiation of spleen plus remainder of the body resulted in spleen weight losses showing a marked dependence on X-ray dosage. He also noticed that the irradiation of the body did not produce spleen weight loss at 5 days when the exteriorized spleen was shielded. By irradiating a portion of abdomen of mice with 20 MeV deuterons, Jansen et al.[6] have shown a decrease of splenic weights at 6 days as a result of an abscopal effects.

On the other hand spleen weight after irradiation decreases rappidly and then recovers with or without overshoot depending upon doses of X-ray.[1,2] The present experiments have covered a time course of atrophy and recovery of spleen weight up to 14 days after irradiation in order to see when any abscopal effect is observed.

Materials and Method

Animals used in the present experiments were ddY/SLC female mice of 10 weeks old. The X-ray

machine was operated at 200 kvp, 20 mA with filters of 0.5 mm Cu and 0.5 mm Al. Dosimetry was done with Farmer substandard dosemeter MK-2 and with lucite phantom of mice. The dose-rate was 38.2 R/min. For partial body irradiation, the following two groups were assigned.

1. Trunk exposure (chest and abdomen)
2. Lower body exposure (pelvis, legs and tail) and trunk exposure

The shield was accomplished with lead 5 mm thick. The absorbed dose in the shielded area was a few per cent of that in the irradiated area. All mice were anaesthetized by intraperitoneal injection of Nembutal during the irradiation. Control mice were also anaesthetized in the same way. In case of combined exposures of trunk and lower body, lower body was exposed to graded doses immediately after exposure of trunk with 1000 R. At each time 8 mice were irradiated. Mice were bred in cages by five in a room equipped with a forced-air ventilation system and the temperature was kept at 24°C. Food and water were given ad libitum. Each mouse was sacrificed at pre-determined time after exposure with celvical dislocation, its spleen was taken out and weighed immediately.

Results

1. Splenic weight after whole body or trunk exposure

Changes of splenic weights after whole body exposure with 500 R or 1000 R were summarized in Table

Table 1. Splenic weights of control mice and of irradiated mice at whole body

Days after exposure (or after anaesthesia)	Control (anaesthetized)		Dose to whole body			
			500R		1000R	
	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)
0	55	111.2 ± 3.5	55	111.2 ± 3.5	55	111.2 ± 3.5
1	8	107.5 ± 5.4	8	42.2 ± 2.0	8	48.9 ± 3.7
2	8	119.6 ± 2.7	8	42.9 ± 3.2	8	39.5 ± 2.9
3	8	120.0 ± 6.7	8	44.6 ± 0.8	8	29.8 ± 1.3
5	8	117.3 ± 4.6	8	46.8 ± 4.3	7	26.0 ± 1.4
7	8	111.0 ± 5.3	7	34.7 ± 3.2	—	———
9	10	116.2 ± 7.1	6	70.2 ± 17.9	—	———
11	—	———	6	102.4 ± 22.9	—	———
14	8	113.6 ± 3.9	7	123.9 ± 11.4	—	———

1. In case of 1000 R exposure to whole body, no data were available beyond 5 days after exposure due to high mortality. The same data as in Table 1 were plotted in Figure 1. Splenic weights of 1000 R group showed no recovery up to 5 days and the weights of 500 R group began to recover at 9 days. The other two curves were taken from the data in Table 2 where splenic weights after lower body exposure with graded doses in addition to trunk exposure of 1000 R were tabulated. Comparing with 500 R group of whole body exposure, the group of trunk exposure with or without lower body exposure showed earlier onset of recovery. As shown in Figure 1, the splenic weights at 7 days show an appreciable amount of recovery in the groups of 1000 R exposure to trunk with or without exposure of lower body. On the other hand, the splenic weights at 7 dya show no recovery at all in the group of 500 R exposure to whole body. The above results may suggest that shield of head and forelegs in the present experiment is responsible to an earlier onset of recovery and that exposure of lower body in addition to trunk exposure has not much influence on

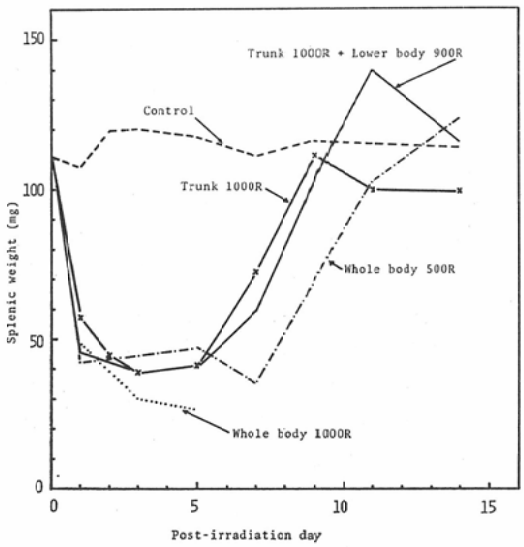

Fig. 1　Changes of splenic weights after whole or partial body irradiation

Table 2.　Splenic weights after lower body exposure with graded doses in addition to trunk exposure with 1000R

Days after exposure	Dose to lower body: 0		200R		300R		400R	
	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)
0	55	111.2 ± 3.5	55	111.2 ± 3.5	55	111.2 ± 3.5	55	111.2 ± 3.5
1	8	57.5 ± 2.9	11	52.8 ± 2.6	11	54.2 ± 2.9	8	48.8 ± 4.4
2	8	44.3 ± 2.1	8	44.0 ± 3.0	8	39.2 ± 2.9	8	40.0 ± 2.6
3	8	38.7 ± 3.0	12	36.8 ± 1.9	11	37.9 ± 1.8	11	35.8 ± 1.7
5	11	40.8 ± 1.6	12	42.0 ± 1.7	12	40.7 ± 1.5	10	42.4 ± 2.3
7	8	72.0 ± 7.0	12	58.1 ± 3.8	14	58.5 ± 4.5	9	51.0 ± 3.2
9	8	111.5 ± 4.9	16	96.9 ± 5.9	15	97.0 ± 8.3	15	97.9 ± 5.5
11	8	100.0 ± 6.9	12	111.0 ± 10.0	11	109.1 ± 9.8	10	120.1 ± 8.0
14	10	99.4 ± 7.1	11	111.6 ± 9.7	11	108.6 ± 5.9	8	108.1 ± 6.1

Days after exposure	Dose to lower body: 500R		700R		900R	
	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)	No. of mice	Mean ± SE (mg)
0	55	111.2 ± 3.5	55	111.2 ± 3.5	55	111.2 ± 3.5
1	8	49.3 ± 3.4	10	53.0 ± 3.8	8	45.2 ± 2.3
2	8	47.2 ± 3.6	8	44.1 ± 2.1	11	42.2 ± 2.7
3	10	39.3 ± 2.4	12	38.0 ± 2.3	12	39.1 ± 1.6
5	11	41.4 ± 1.7	12	40.5 ± 1.8	12	40.2 ± 2.3
7	11	54.1 ± 1.9	14	56.8 ± 3.1	13	59.7 ± 5.6
9	16	97.8 ± 7.5	15	116.1 ± 13.4	16	104.3 ± 7.2
11	11	120.1 ± 7.0	12	144.1 ± 8.4	10	139.6 ± 8.6
14	12	122.9 ± 7.3	10	117.4 ± 5.9	12	115.3 ± 5.6

onset of recovery.

2. Splenic weight after lower body exposure in addition to trunk exposure of 1000 R.

Table 2 shows complete data of the groups which received graded doses of X-ray to lower body immediately after exposure of 1000 R to trunk. Some of the data in Table 2 were plotted in Figure 2. Other data were not plotted in Figure 2, simply because they showed similar patterns in the changes. As was seen in Figure 2, changes of splenic weights were approximately independent of the doses to lower body up to 7 days after irradiation. An apparent dependence on the doses of lower body was seen at 11 days after

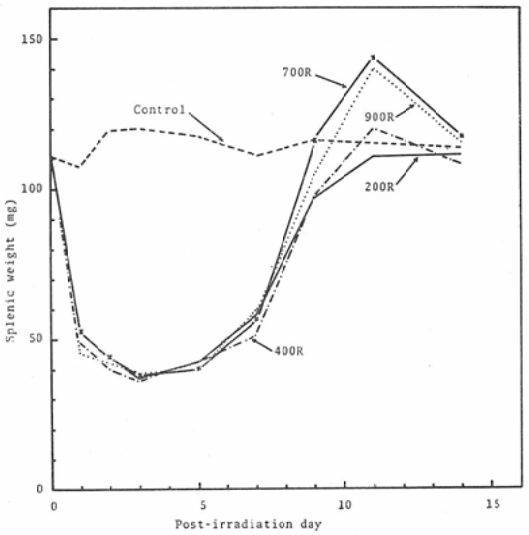

Fig. 2. Changes of splenic weights by lower body exposure immediately after 1000 R to trunk. Doses given to the curves indicate doses to lower body.

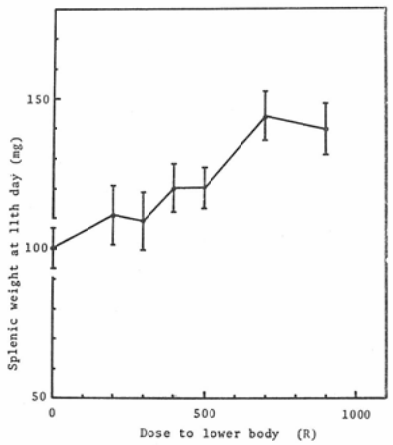

Fig. 3. Splenic weights at 11 days after lower body exposure with 1000 R to trunk.

irradiation when most of groups showed maximum recovery. As was shown in Fig. 3, the splenic weights at 11 days increased with the doses of lower body up to 700 R. The groups of higher doses showed a phenomenon of over-recovery (See Figure 2). Accordingly abscopal effects of irradiated lower body on splenic weights were not observed until 7 days after irradiation in our exposure patterns. It may be concluded that doses to lower body in addition to 1000 R to trunk have influence on maximum recovery at 11 days after irradiation.

Discussions

It is well known that a shield of the spleen highly reduces the mortality of acute death.[3] Histological studies on bone marrow clarified that a shield of the spleen enhanced a recovery in the bone marrow[5]. And also a shield of the spleen prevented mice from anemia[4]. On the other hand heavy irradiation to the exteriorized spleen did not produce hematopoietic death[10].

The evidences mentioned above suggest that the functions of the spleen are closely related to the functions of the bone marrow. In effect Kurnick et al.[7] have given an interpretation that the constant circulation of bone marrow elements in the mouse may account for the abscopal effects of X-irradiation. The

data given in Figure 3 show a larger recovery at 11 days with larger doses to lower body. With whole body irradiation Brues et al.[1] also noticed that the overshoot of the splenic weights at 17 days was larger in the groups of larger doses. If a larger dose to lower body in our experiments stimulates the circulation of bone marrow elements to larger extent, Kurnick's interpretation may not be inconsistent with the results given in Figure 3.

Summary

Changes in splenic weights were observed up to 14 days after whole or partial body irradiation. The weights of a group received 500 R to whole body began to recover at 9 days. On the other hand, the splenic weights of groups received 1000 R to trunk with or without lower body exposure showed an earlier onset of recovery than that of 500 R to whole body. In order to observe an abscopal effects of irradiated lower body on the splenic weights, some groups of mice received graded doses to lower body immediately after 1000 R exposure to trunk. In the groups of above combined exposures, changes of splenic weights were approximately independent of the doses to lower body up to 7 days after irradiation. The doses to lower body have influence on maximum recovery at 11 days after irradiation. The splenic weights at 11 days increased with the doses to lower body up to 700 R.

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