LETHAL SHOCK IN IRRADIATED RABBITS IN RESPONSE TO ADMINISTRATION OF HOMOLOGOUS γ -GLOBULIN

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Many pathological processes are accompanied by a change in the quantity of one or another serum protein, which is reflected in the ordinary protein-fraction ratio and the globulin-albumin index. These indices are widely used in diagnostics. However, quantitative changes in protein content, apparently on reaching "critical" levels, may themselves cause new reactions in certain of the body's reactive systems, especially when the latter are also altered, as is the case, e.g., in radiation sickness.

In the present work we studied the influence of an artificial increase in serum γ -globulin content on irradiated rabbits.

EXPERIMENTAL METHOD

The γ -globulin was obtained from the serum of rabbits vaccinated with B. Breslau by salting-out with ammonium sulfate. The dried preparation was wetted with 1 ml per 5 mg of a 0.85% NaCl solution and then passed through a Zeitz filter. Healthy rabbits withstood intravenous injections of 50 mg of γ -globulin well. This dosage was also used in the experiments.

Rabbits weighing 2.5-3 kg were irradiated in pairs with 3 tubes of a 12-tube x-ray apparatus under the following conditions: 180 kv, 14 ma, 0.5 mm Cu + 1 mm Al filter, target distance 60 cm, dose rate 35.7 r/min, total dose 800 r.

EXPERIMENTAL RESULTS

Irradiation causes rabbits to develop acute radiation sickness involving characterstic changes in the white blood, a hemorrhagic syndrome, symptoms of microbial invasion (in the form of bacteriemia, pneumonia, and other infection complications), and loss of weight; this usually leads to 30% mortality within 30 days. Death from radiation shock, frequently observed on irradiation in larger doses, is very rarely noted in rabbits on irradiation in a dose of 800 r.

We irradiated 6 rabbits in the 1st series of experiments. The first pair of rabbits reacted very severely to protein administered 1 h after irradiation. They soon became sluggish, exhibited dyspnea, stretched out on their stomachs, and were unable to stand erect when prompted to do so. They then collapsed on their backs and lay in a manner resembling complete prostration. Finally, the rabbits developed severe convulsive twitching of the extremities, their heads retracted, and they gave piercing screams and died. This pattern is typical of shock in this species of animal. One rabbit died 22 min and the other 39 min after injection of the protein.

In order to demonstrate conclusively that death resulted from our intervention, we injected still another rabbit 1 h after irradiation. This rabbit died 38 min after administration of the γ -globulin, exhibiting the same symptoms. The 3 remaining irradiated rabbits were in satisfactory condition at this time.

Taking into account the data on the varying reactivity of the organism during different phases of radiation sickness [2], we assumed that an intolerance to excess homologous protein is set up shortly after irradiation.

Development of Acute Shock in Irradiated (800 r) Rabbits after Administration of 50 mg of Homologous γ -Globulin

Rabbits	No. of Rabbits	γ -globulin preparation administered	Manner of administration	Interval between irradiation and administration	Reaction of organism 1 day after irradiation
Unirradiated	4	Isolated from immune serum (anti-Breslau)	Intravenous	—	Acute shock did not develop; all the rabbits survived
Irradiated	7	The same	The same	1 h	Acute shock developed; all the rabbits died of shock, after 6, 22, 27, 38, 39, and 128 min and 10 h respectively
"	3	" "	" "	3 days	Acute shock did not develop; all the rabbits survived
"	3	" "	Intramuscular	1 h	The same
"	2	Isolated from the serum of rabbits which survived irradiation in a dose of 800 r	Intravenous	The same	Acute shock developed in 1 rabbit, which died 7 min after injection
"	3	The same	Intramuscular	" "	Acute shock did not develop; 1 rabbit died during the 1st day after irradiation
"	2	Physiological solution	Intravenous	" "	Acute shock did not develop; both rabbits survived

We were convinced of the validity of this assumption when we injected the 3 remaining rabbits with the same dose of γ -globulin intravenously 3 days after irradiation. They had already developed radiation leucopenia at this time. Nevertheless, they did not die of shock after the γ -globulin injection. This obviously indicated that the reaction of the irradiated organism varies in accordance with the phase of radiation sickness. It must be pointed out that Shwartzman's phenomenon cannot be induced in rabbits 3 days after irradiation in a dose of 800 r [1, 4].

It was necessary to determine the importance of the manner in which the γ -globulin was administered and to compare the effect observed with the reaction to injection of another γ -globulin preparation.

In the 2nd series of experiments the rabbits were injected intravenously (a repetition of the previous experiment) and intramuscularly with the same quantity of immune γ -globulin 1 h after irradiation in a dose of 800 r. For purposes of comparison we administered γ -globulin prepared by the same method from the serum of rabbits which survived for 2 months after irradiation in a dose of 800 r.

It was found that the manner in which the γ -globulin is administered plays an important role. In these experiments the rabbits which received intravenous injections displayed the shock pattern described above: all 4 rabbits died after administration of immune γ -globulin, while 1 of 2 animals died after administration of γ -globulin isolated from the serum of irradiated rabbits. Intravenous injection of 10 ml of physiological solution and intramuscular injection of these same proteins did not produce shock or death within the first few days after administration. The table summarizes the data obtained in these 2 series of experiments.

Both intravenous and intramuscular injections of homologous protein had a leucopenic effect and, with rare exceptions, caused a decrease in body temperature. However, in lethal cases these phenomena were progressive; this confirms the development of shock.

In considering the phenomena observed one is first struck by the thought that homologous γ -globulin may be altered during salting-out with ammonium sulfate. However, a comparative study of the properties of the γ -globulin preparations isolated by 5 different methods, including salting-out with ammonium sulfate, showed [5] that γ -globulin prepared by this method acquires unusual characteristics; the absence of denaturation must be specially emphasized.

The γ -globulin solutions were filtered through a bacterial filter, which kept large dispersed particles from entering the solutions to be administered. That there were no small-scale changes in the protein may be seen from the fact that conversion of immune serum to immune γ -globulin did not affect antibody specificity. In our opinion, this strongly indicates that the protein retains its structure when brought into contact with ammonium sulfate.

We believe that the data obtained show that a sharp rise in the γ -globulin content of the blood plays an important role in the development of shock. This content probably does not reach critical levels on intramuscular injection [3].

SUMMARY

A solution of homologous γ -globulin (50 mg in 10 ml of physiological saline) was injected intravenously in rabbits 1 h after the irradiation with 800 r. Eight of 9 rabbits died of shock soon after the injection, although the same dose of the preparation did not result in shock when injection was administered 3 days after exposure to irradiation of healthy animals. The author explains the findings by a varying reactivity of the irradiated organism at various phases of radiation sickness, and by the importance of higher γ -globulin concentrations in the blood for the advent of shock.

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