EFFECT OF PARTIAL HEPATECTOMY ON IMMUNE RESPONSE IN ANIMALS

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UDC 612.017.1-06:612.35-089

Production of hemagglutinins and hemolysins is increased in rabbits immunized with sheep's erythrocytes during regeneration of the liver after partial hepatectomy compared with intact animals and animals undergoing a mock operation.

The investigation of various aspects of regeneration of the liver after partial hepatectomy has a direct bearing on problems in general and applied immunology. A particularly important aspect is the study of immunological changes in the body after hepatectomy, because immunological mechanisms are evidently responsible for regulation of regeneration in the organ after partial resection.

In the investigation described below the immune response of rabbits was studied after partial hepatectomy.

EXPERIMENTAL METHOD

The experimental animals were 22 chinchilla rabbits weighing 2.3-2.5 kg. The left lobe of the liver (35-40% of the total mass of the organ) was removed from 8 experimental rabbits; 7 animals underwent a mock hepatectomy, and no operation of any kind was performed on 7 rabbits. The animals of all 3 groups were immunized intravenously with 1 ml of a 10% suspension of sheep's erythrocytes on the 3rd day after the operation. The 2nd injection of antigen was given after 48 h in the same dose. Immunization coincided with the period of maximal mitotic activity of the liver cells [4].

EXPERIMENTAL RESULTS

The experimental results are given in Table 1.

In rabbits undergoing partial hepatectomy, a considerable increase in intensity of the immune response was observed: the blood antibody level of the experimental animals was more than 3 times higher than in animals undergoing the mock operation and in intact rabbits; at all periods of the investigation the difference was statistically highly significant ($P < 0.01$-0.001). The mock operation did not stimulate production of hemagglutinins and hemolysins (difference between titers of antibodies not statistically significant). In the hepatectomized animals, the blood antibody concentration reached its maximum sooner; whereas in intact rabbits and rabbits undergoing the mock operation the maximum occurred on the 11th day after the 2nd injection of antigen, in hepatectomized rabbits it occurred on the 7th-9th day.

Increased production of hemolysins in partially hepatectomized rats was also observed by Havens et al. [6], but these workers immunized the animals immediately after the operation, which is not justified methodically because injection of the antigen under these circumstances was given 2 days before the maximum of mitotic activity in the liver of the hepatectomized rats [3].

Department of Biochemistry, Kursk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR O. V. Baroyan.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 70, No. 9, pp. 61-63, September, 1970. Original article submitted January 22, 1970.

TABLE 1. Blood Antibody Titers of Hepatectomized and Control Rabbits at Various Times after Immunization with Sheep's Erythrocytes

Group of animals	Titer of normal antibodies	Day after 2nd injection of antigen					
		5th	7th	9th	11th	13th	15th
		Hemagglutinins					
Hepatectomized	13	8 190	25 250	21 240	19 470	12 630	7 511
Undergoing mock hepatectomy	12	105	4 512	4 512	7 420	1 680	1 024
Undergoing no operation	13	116	4 096	3 710	6 719	1 855	927
		Hemolysins					
Hepatectomized	103	23 470	46 950	51 190	39 480	25 600	16 600
Undergoing mock hepatectomy	88	3 900	14 140	17 230	17 230	10 500	4 306
Undergoing no operation	88	4 306	12 800	15 610	17 230	10 500	3 900

Note. Geometric mean titers of antibodies given in this table.

It can be concluded from these experimental results that increased proliferation not only in the liver, but also in the lymphoid organs responsible for production of immunoglobulins and antibodies, takes place in animals after partial hepatectomy.

The humoral or "immunologic" factor regulating growth or regeneration of the liver after injury to the organ is known to be synthesized in the liver itself [7]. It has also been shown that the blood plasma of animals during the first few hours after partial hepatectomy, if injected into intact animals, stimulates mitotic activity of the liver cells [5]. However, the specificity of action of the humoral factor is not absolute: after partial hepatectomy mitotic activity is increased not only in the liver, but also in the cornea, kidney, and salivary gland [1, 2, 9]. It is natural, therefore, to suggest that proliferation of lymphoid tissue in which immunoglobulins are formed also is increased in hepatectomized animals. This is confirmed by the recent discovery [8] of an increase in the rate of DNA synthesis in cell nuclei of lymphoid tissue after partial hepatectomy, with a maximum on the 3rd day after the operation.

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