EFFECT OF SPLENECTOMY ON REGENERATION OF THE LIVER IN DOGS

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Experiments on dogs have shown that splenectomy appreciably reduces the rate of recovery of the weight of the liver after partial resection of its parenchyma. Whereas 90.3% of the resected mass of the organ in healthy dogs was restored one month after resection of the left lobe, only 70.4% of its mass had been restored by the same time.

Recent experimental work and clinical observations have demonstrated the close link between the functions of spleen and liver. Splenectomy disturbs the cholesterol-synthesizing activity of the liver and its ability to oxidize tyrosine and to bind phenols, reduces the rate of protein renewal in the liver tissue, and so on [1-3].

Existing data on the effects of splenectomy on regeneration of the liver are few in number of conflicting in nature. Di Domizio and Caviceni [4] and Kratochvil and Vnukova [7], for example, who studied the rate of recovery of the liver weight after splenectomy, found that this operation reduces the ability of the liver to regenerate. Paratello and co-workers [8] found no connection between the presence or absence of the spleen and the rate of liver regeneration. On the other hand, Jonescu and Cracin[5] state that regeneration of the liver in rats is accelerated by simultaneous splenectomy. Most workers who have studied this phenomenon have estimated the regenerative power of the liver simply from the rate of restoration of its weight and they have not studied either the morphological or the functional state of the organ.

To clarify these matters, experiments were carried out on 49 sexually mature noninbred dogs. The left lobe of the liver was resected in 34 of these animals (control group) and the character of the morphological and functional changes in the liver was studied. In the other 15 animals, resection of the liver was accompanied by splenectomy.

EXPERIMENTAL

Animals weighing from 11.5 to 13 kg, with a mean weight of 12.5 ±0.2 kg, were used in the experiment.

In five control dogs with body weight 12.5 kg the weight of the liver was 437.5 ±21.0 g, and the left lobe weighed 168.3 ±9.4 g, or 36.4% of the total weight of the organ.

The operation was performed under endothracheal ether anesthesia, with aseptic precautions. The abdomen was opened through a Topchibashev's incision in the 10th right intercostal space. The spleen was removed after preliminary ligation of the vascular pedicle. Next, after division of the left triangular ligament, the left medial and lateral lobe of the liver were brought into the wound. A silk ligature was applied to each lobe separately at its base, and the lobes were resected and immediately weighed. The omentum was brought to the wound surface. The abdominal and thoracic wounds were sutured in layers without drainage.

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TABLE 1. Functional Changes in Dogs after Resection of Left Lobe of Liver

Index	Before operation	After operation				
		3rd day	7th day	14th day	21st day	28th day
No. of animals	25	25	20	15	10	5
Total serum of protein (in g%)	8,24±0,69	7,1±0,42	6,9±0,74	6,9±0,68	7,85±0,66	7,2±0,28
Albumins (in g %)	3,97±0,27	2,77±0,29	2,33±0,31	2,91±0,2	3,54±0,71	3,44±0,11
Globulins (in g %)	4,27±0,19	5,33±0,33	4,57±0,19	2,99±0,2	4,31±0,20	3,67±0,3
A/G ratio	0,96±0,01	0,58±0,02	0,5±0,03	0,69±0,03	0,77±0,02	0,9±0,05
Bromsulphalein retention (in %)	4,2±0,2	10,1±0,18	17,1±0,3	14,0±0,35	8,5±0,26	5,9±0,31
Prothrombin index (in %)	101,2±2,3	82,0±3,1	84,9±3,7	98,0±3,2	117,1±2,8	109,6±2,7

TABLE 2. Functional Changes in Dogs after Resection of Left Lobe of Liver and Simultaneous Splenectomy

Index	Before operation	After operation			
		3rd day	7th day	14th day	28th day
No. of animals	12	12	9	6	3
Total serum protein (in g %)	7,3±0,5	7,1±0,4	7,0±0,5	7,1±0,3	7,45±0,5
Albumins (in g %)	3,66±0,3	2,38±0,2	1,82±0,18	1,37±0,16	2,5±0,2
Globulins (in g %)	4,24±0,25	4,72±0,2	5,18±0,3	5,73±0,3	4,98±0,2
A/G ratio	0,9±0,01	0,5±0,02	0,35±0,01	0,25±0,03	0,5±0,03
Bromsulphalein retention (in %)	3,2±0,2	10,6±0,7	14,2±0,5	13,4±0,7	4,6±0,8
Prothrombin index (in %)	100,2±0,7	82±0,8	53±0,8	57±0,6	74±0,8

Functional and morphological investigations were carried out on the 3rd, 7th, 14th, and 28th days after the operation. Immediately after sacrifice, the liver was removed and weighed. A piece of tissue was taken for histological investigation. The serum concentration of protein and protein fractions was determined, the bromsulphalein test of liver function carried out, and the prothrombin index estimated.

EXPERIMENTAL RESULTS

After resection of the left lobe of the liver a gradual but fairly rapid increase in weight of the organ was observed in the control animals. This increase was particularly marked in the first two weeks. On the third day after the operation 28.3 ± 0.4% of the mass of the liver was restored, 49.2 ± 0.7% on the 7th day, 77.1 ±0.5% on the 14th day, and 90.3 ±0.6% by the end of one month; the weight of the liver by this time had reached 96.78 ±0.6% of its initial weight.

In splenectomized animals the rate of growth of the liver tissue was slower. On the third day after operation the mass of the liver was restored by 25.2 ±0.3%, on the 7th day by 37.1 ±0.7%, and on the 14th day by 56.9 ±0.3%. By the end of the month only 70.4 ±0.6% of the resected mass of the liver had been restored.

These experiments thus confirmed the views of Di Domizio and Caviceni [4] and Kratochvil and Vnukova [7] that splenectomy reduces the ability of the liver to recover its weight.

The reasons for this phenomenon are largely unclear. One interesting fact must be mentioned. The dogs tolerated resection of the liver better if the spleen was removed at the same time. For example, nine of the 34 animals (26%) undergoing resection of the left lobe of the liver died, whereas of the 15 dogs from which the spleen was removed at the same time, only one died in the postoperative period. This was also reflected in the character of the morphological changes in the organ, especially during the first few days after the operation.

On the 3rd day after resection of the liver, for instance, the organ was considerably congested with blood, and in some places blood-filled lacunae were formed. Dilatation of the central veins and intercolumnar capillaries was observed. Stasis was particularly marked in the subcapsular zones. Although the lobular and columnar structures of the organ were undisturbed, considerable cloudy swelling and fatty degeneration of the liver cells could be seen. In the later stages, these signs of a disturbed circulation became less severe, and cells of different sizes and shapes appeared. By the end of the second week, hepatic lobules of different sizes could be clearly distinguished. Areas consisting of irregularly shaped liver cells with large, hyperchromic nuclei were found. Pale (young) ill-defined liver cells, among which were larger hepatocytes of different sizes with a strongly oxyphilic cytoplasm, were frequently observed. Some cells had two or three nuclei. These were particularly numerous by the end of the 4th week.

In the splenectomized dogs the picture of disturbed circulation and congestion was much less marked. On the third day after operation congestion of the liver was moderately severe. The liver cells had large, hyperchromic nuclei, but no signs of cloudy swelling. Although in the subcapsular zones cells with pale and ill-defined cytoplasm could be seen, and polymorphism of the cells was present. These characteristics were much less marked. Large hepatocytes with two or three nuclei were more frequent.

Hence, in the postoperative period after resection of the liver and simultaneous splenectomy, much less severe morphological changes were found in the liver. The degree of cloudy swelling and fatty degeneration was much lower.

On the other hand, as described by Jonescu and Cracin [5], absorption of the necrotic areas of the liver in the region of the stump occurred much more rapidly in the dogs of this series; scar adhesions between the greater omentum and liver tissue were formed much sooner and were more conspicuous.

The results of liver function tests are given in Tables 1 and 2.

Analysis of the biochemical data for these groups of animals shows that in the dogs undergoing resection of the left lobe of the liver and simultaneous splenectomy, the ratio between the serum protein fractions was more severaly disturbed, and the disturbances were more prolonged. Although the total serum protein content in the postoperative period showed little change in these animals, marked deviations were found in the content of the protein fraction. The albumin content showed a decrease at all times of investigation. Towards the end of one month the albumin content was slightly increased, but still remained below its initial level. Conversely, the content of globulin fractions was increased. Disturbances of the ratio between the serum protein fractions were particularly severe in the splenectomized animals on the 7th-14th day, when the albumin-globulin ratio was 0.3-0.2.

Appreciably more severe changes in this group were also observed when the prothrombin index was studied. This was regularly decreased in the postoperative period. Even at the end of the investigation the prothrombin index was 74-76%. The bromsulphalein test showed no particular difference between the groups studied.

It can thus be concluded from these results that splenectomy reduces the rate of restoration of the weight of the liver after partial resection of its parenchyma. This effect was apparently due to depression of the proliferative response of the liver cells through a decrease in the inflow of portal blood into the liver. This hypothesis is confirmed by the general character and specific features of the histological changes in the postoperative period.

On the other hand, the reason for the decrease in regenerative power of the liver after splenectomy evidently must also lie in a disturbance of the correlative associations between these two organs. Biochemical tests show that after splenectomy a more severe and more prolonged disturbance of the protein-synthesizing function of the liver takes place after resection of its left lobe.

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