Morphometric Characteristics of Liver Acini in Dogs with Acute Cholecystitis

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Morphometric analysis of the liver in dogs with acute cholecystitis revealed specific alterations in liver acini in various forms of acute cholecystitis.

Key Words: *liver acinus; morphometry; cholecystitis*

Impairment of liver function is a frequent cause of postoperative complications and early postoperative mortality in patients with acute cholecystitis [9]. The main pathogenetic factors of hepatic failure is intoxication of a complex origin directly and indirectly damaging liver cells [2,3,10]. This paper presents the morphometric characteristics of liver acini in various forms of acute cholecystitis.

MATERIALS AND METHODS

Experiments were carried out on 36 mongrel dogs with acute experimental cholecystitis. A modified experimental model proposed by V. S. Shevchenko was used [6]. In brief, a catgut ligature was applied to the cystic duct and 2-fold dose of staphylococcal culture in normal saline was injected into the gallbladder through an insulin needle. The animals were sacrificed after 1, 3, 5, and 7 days. Control group consisted of sham-operated animals (laparotomy and suturing of the abdominal cavity). All experiments on animals were carried out in accordance with the "Regulations of Manipulations on Experimental Animals". Liver fragments from the right lateral lobe were embedded in paraffin, the sections were stained with hematoxylin and eosin. The areas of nuclei and cytoplasm, area and perimeter of sinusoids were measured in the 1st (periportal) and 3rd (perivenular) zones of liver acini using a MEKOS-C analyzer in accordance with routine rules of liver tissue morphometry [1,7,11]. From these values, the hepatocyte nucleus/cytoplasm ratio and a factor of sinusoid shape were estimated.

The data were statistically processed using Student's t test.

RESULTS

Microscopy of the liver of control dogs showed slight uneven sinusoidal plethora, moderate granularity of the cytoplasm, and solitary monocellular necroses in the perivenular zones of acini, which were not manifestations of disease and can be observed in healthy animals. The detected morphological changes in dog liver in destructive forms of acute cholecystitis corresponded to the picture of the so-called nonspecific reactive hepatitis (NRH), which was in line with published data [4]. Morphological changes in phlegmonous cholecystitis developing on day 3 of the experiment were classified as lobular NRH of minimum activity with predominant involvement of the perivenular acinus zone.

On day 5 phlegmonous ulcerative cholecystitis developed in the gallbladder wall. Morphological picture of low-active lobular NRH was observed in liver tissue during this period. Day 7 of experiment was characterized by the development of phlegmonous gangrenous cholecystitis in the gallbladder wall; changes in the liver could be classified as moderately active lobular NRH. No pathognomonic signs of liver damage were detected in different forms of acute cholecystitis in the examined animal groups. Microcirculatory disorders, reversible and irreversible damage of

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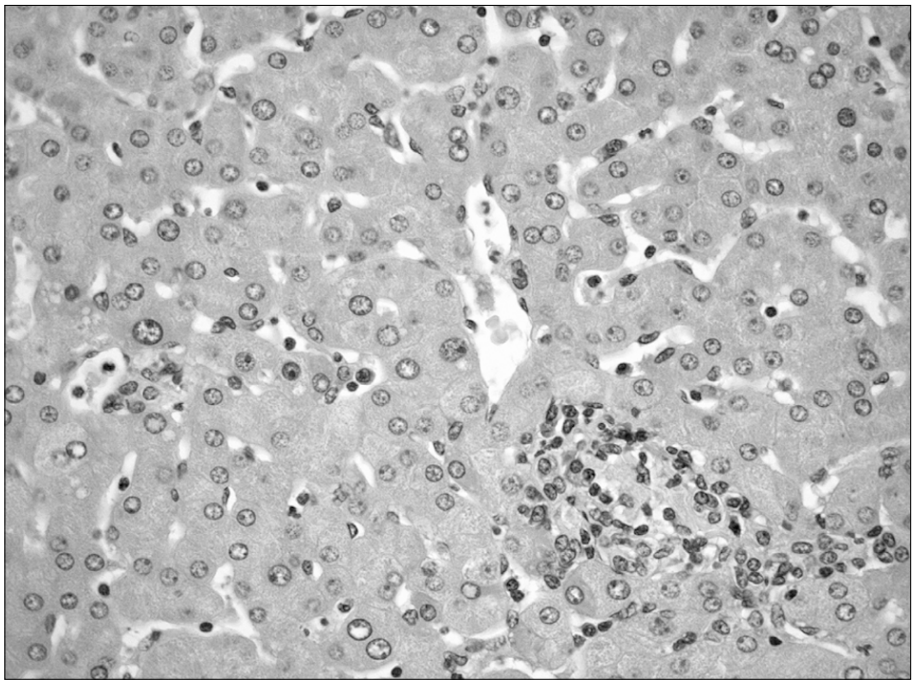

Fig. 1. Small focal necrosis in the 3rd zone of liver acinus in dogs (day 3 of experiment). Hematoxylin and eosin staining, ×400.

mainly perivenular and partially intermediate hepatocytes (Figs. 1, 2), lymphohistiocytic infiltration of portal tracts were seen in all the cases. Periventricular and triangular necroses in liver parenchyma were detected in phlegmonous ulcerative and phlegmonous gangrenous cholecystitis, in the portal tracts the inflammatory infiltration crosses the terminal plate and forms ladder necroses (Fig. 3).

For a more precise quantitative evaluation of liver tissue damage, morphometrical analysis of liver acini was carried out. In control animals the area of hepatocyte nuclei and the area and perimeter of sinusoids were higher in the perivenular zone, which confirmed published data on structural heterogeneity of liver acini [3]. Deviations of the studied parameters from the control values were observed in the liver of experimental animals with acute cholecystitis (Table 1).

On day 1 of the experiment the area of hepatocyte nuclei increased by 3.7% in the 1st zone and decreased by 1.2% in the 3rd zone in comparison with the con-

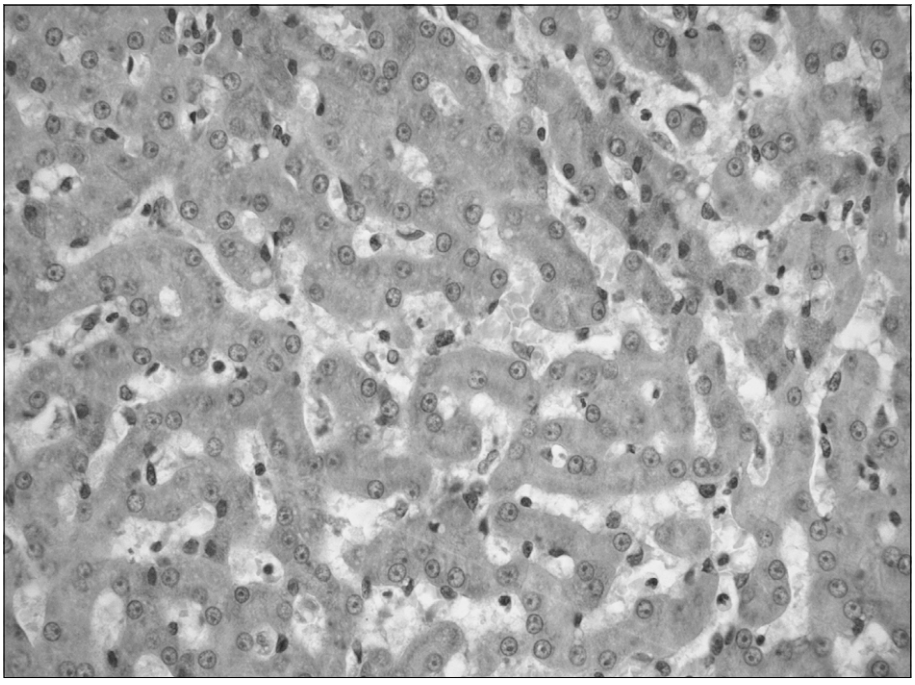

Fig. 2. Dilatation and plethora of sinusoids in the 3rd zone of liver acinus (day 5 of experiment). Hematoxylin and eosin staining, ×400.

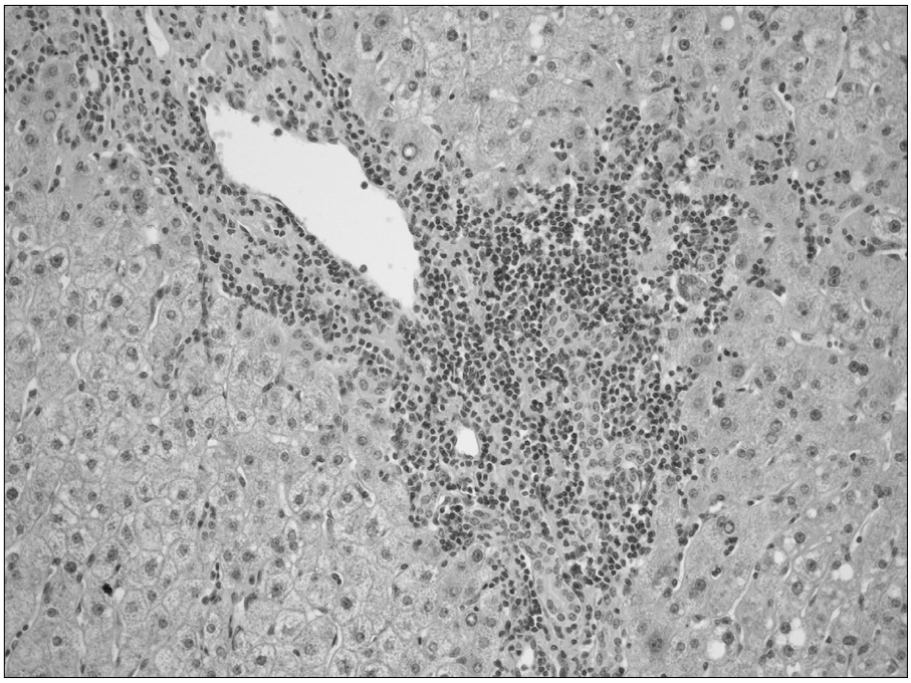

Fig. 3. Spreading of inflammatory infiltration beyond the terminal plate (day 7 of experiment). Hematoxylin and eosin staining, ×200.

trol (differences are insignificant), which can be due to intensification of metabolic processes in cells. The area of nuclei decreased starting from day 3 of the experiment, and on day 5 the area of the hepatocyte cytoplasm also decreased. The maximum decrease in these parameters was detected in the perivenular zone of liver acini, where degenerative and necrotic processes progressed. The increase in nuclear area and decrease of cytoplasm area in periportal cells on day 7 probably attests to reparative regeneration.

The area and perimeter of sinusoids in animals with acute cholecystitis underwent phasic changes. On days 1, 5, and 7 of the experiment the area and perimeter of sinusoids increased mainly in the perivenular zones of liver acini in comparison with the initial values. The maximum changes in these parameters were

TABLE 1. Morphometric Characteristics of Liver Acini in Dogs with Acute Cholecystitis (*M*±*m*)

Day of experiment	Zone	S_1	S_2	S_1/S_2	S_3	P	$P2/S_3$
Control	1	4221±136	18 068±241	0.23	43 623±1085	16 156±309	5983±0.45
	3	4517±138	17 563±219	0.25	45 262±1126	17 464±317	6738±0.35
	C	0.93	1.02		0.96	0.92	
1st	1	4377±142	17 885±216	0.24	44 081±1142	164 828±311	6122±0.34
	3	4463±145	17 097±209	0.26	47 347±1147	18 203±319	6998±0.31
	C	0.98	1.04		0.93	0.90	
3rd	1	4262±137	18 127±243	0.24	43 977±1114	16 365±311	6089±0.84
	3	4113±124	17 348±218	0.23	46 693±1138	17 976±317	6920±0.45
	C	1.01	1.04		0.94	0.91	
5th	1	4139±125	18 002±237	0.23	44 151±1146	16 489±311	6158±0.11
	3	3985±122*	17 246±217	0.23	52 013±1201*	18 433±321*	6532±0.06
	C	1.03	1.04		0.85	0.89	
7th	1	4273±137	17 929±227	0.24	45 971±1174	16 752±312	6104±0.48
	3	3982±121*	17 212±212*	0.23	55 284±1185	19 539±337*	6905±0.66
	C	1.07	1.05		0.83	0.86	

Note. *1*) periportal zone; *3*) perivenular zone; *C*: periportal-perivenular activity gradient; S_1: area of nuclei; S_2: cytoplasm area; S_1/S_2: hepatocyte nuclear/cytoplasmatic ratio; S_3: sinusoidal area; *P*: sinusoidal perimeter; P^2/S_3: sinusoidal shape factor. *$p<0.05$ compared to the control.

observed on day 7, which was confirmed by histological examination showing dilatation and plethora of sinusoids at this term. On day 3 the area and perimeter of sinusoids decreased in comparison with day 1 most likely due to hepatocyte swelling. The shape factor of sinusoids increased because of the increase in their area and perimeter, especially in the perivenular acinus zone. This parameter also underwent phasic changes, which can be regarded as a compensatory adaptive mechanism in microcirculatory disorders and development of local hypoxia of the organ.

The progress of inflammatory destructive processes in the gallbladder wall was paralleled by changes in the liver, morphologically manifested as NRH. The development of NRH in destructive forms of acute cholecystitis can be regarded as the initial stage of liver involvement, because the main components of its development are impairment of the barrier and detoxification functions of the liver and release of products of impaired cell metabolism into circulation [5]. The presence of suppurative process leads to exhaustion and discoordination of the compensatory adaptive processes. The development of hepatic failure is the main cause of postoperative complications and lethal outcomes in acute cholecystitis [8]. Liver failure in surgical patients develops primarily during the postoperative period. Liver dysfunction leads to development of various postoperative complications (pneumonia, peritonitis, internal hemorrhages, failure of sutures, wound suppuration, *etc.*). Liver dysfunction is associated with impaired resistance to infection, slow wound healing, increased capillary permeability, and blood clotting abnormalities. Clinically, liver function has a certain impact on thanatogenesis, even in cases when hepatic failure is not the immediate cause of death.

Hence, the development of acute cholecystitis leads to disorders in liver structure underlying its dysfunction and playing a certain role in the disease outcome. Morphometric analysis revealed peculiarities of these disorders in various zones of liver acini.

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