Morphological Changes in Hepatic Vessels during Modeling of Pulmonary Trunk Stenosis and after Its Elimination

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Experiments on dogs showed that pulmonary trunk stenosis increased the tone of arterial vessels in the liver and led to the development of veno-arterial and veno-venous reactions. The number of vessels with intimal musculature and myoelastic sphincters in the arterial bed increases, and muscle rolls in large hepatic veins are thickened. The walls are hypertrophic in all vessels. Elimination of the defect abolished the previously formed vascular adaptation reactions, the tone in afferent liver vessels decreased, which leads to regression of hypertrophic changes in their tunica media. The number of arteries with intimal musculature and sphincters decreases. Muscle rolls in the efferent hepatic veins are thinned.

Key Words: *pulmonary trunk stenosis; morphology of hepatic vessels; compensation; reversibility*

Pulmonary trunk stenosis (PTS) is a prevalent congenital heart disease [2,3,5,9]. If the defect is not timely corrected, the patients develop heart failure, the time of its development depending on PTS degree and compensatory potential of the heart and vascular systems in various organs, including the liver [4]. Surgical treatment of patients does not always lead to positive clinical results [3]. The outcomes of surgery are largely determined by the severity and reversibility of structural changes in the arteries and veins of vital organs by the moment of the intervention.

We studied the peculiarities of vascular restructuring in dog liver during experimental PTS and detected signs of regression of this restructuring after elimination of the defect.

MATERIALS AND METHODS

Pulmonary trunk stenosis was modeled in 35 puppies [4,6]. The animals were observed for 6-12 months, after which 25 of them were sacrificed. The artificially created PTS was eliminated in the remaining 10 animals and they were sacrificed after 6-12 months. The material from 10 age-matched dogs served as the control. The animals were sacrificed by bleeding from the femoral artery under ether narcosis in accordance with Regulations for Handling Experimental Animals.

Fragments were excised from different compartments of the liver and fixed in 10% neutral formalin. Histological sections were stained with hematoxylin and eosin, after Masson, Hart, and impregnated with silver after Foot. The afferent blood vessels (branches of hepatic artery, HA, and portal vein) and the efferent vessels (branches of the hepatic vein, HV) were studied by complex morphometry of the hepatic vascular bed [4,7]. In accordance with this method, all HA were divided into 4 groups: large (outer diameter $\geq$125 μ), medium (124-51 μ), small (50-21 μ), and arterioles ($\leq$20 μ). The portal veins were distributed into 4 levels, depending on the diameter of accompanying arteries: veins of the level of large ($\geq$190 μ), medium (189-110 μ), and small (109-51 μ) arteries, and venules

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(arteriole level, ≤50 μ). HV were also classified into 4 types (large, medium, small, venules) in accordance with the the diameter of the corresponding portal veins.

Morphometry of HA and HV was carried out using a screw ocular micrometer [1]. The outer diameters were measured without consideration for the adventitia and tunica media thickness. In addition, small arteries containing bundles of obliquely longitudinal smooth muscles in the intima and arteries with myoelastic sphincters were counted, and the thickness of muscle rolls at the level of large HV was measured.

The results were considered significant, if the error did not surpass 5%.

RESULTS

The tone of HA in PTS was increased, their lumen was stenosed, and the inner elastic membrane looked plicated (Fig. 1, *a*). The number of small HA with bundles of obliquely longitudinal smooth muscles in the intima increased 10-fold (Fig. 1, *b*), that of arteries with myoelastic sphincters 5-fold (Fig. 2). Myoelastosis of the walls with reticulin, elastic fibers, and smooth myocyte growth in them was detected in the portal vein branches. Hepatic veins were plethoric, with hypertrophic leiomyocytes of the muscle rolls protruding into the lumen (Fig. 1, *c*).

Morphometry objectively showed the vascular system of the liver in animals with PTS. The thickness of large HA media increased 1.7 times, of medium and small HA 1.2 times, and of arterioles negligibly (Table 1). The thickness of the walls in the portal veins, accompanying large HA, increased 2.3 times, of those accompanying medium arteries 1.4 times, and of those accompanying small arteries 1.2 times; the walls of the veins of the arteriolar level thickened 1.5 times (Table 1). More significant changes were observed in the efferent HV. The thickness of the media in large veins increased 5-fold, in medium veins 2.1 times, in small veins 1.6 times, and in venules 1.7 times (Table 1). The mean thickness of muscle rolls in large HV increased from 36.0±3.5 to 50.0±3.4 ($p<0.001$).

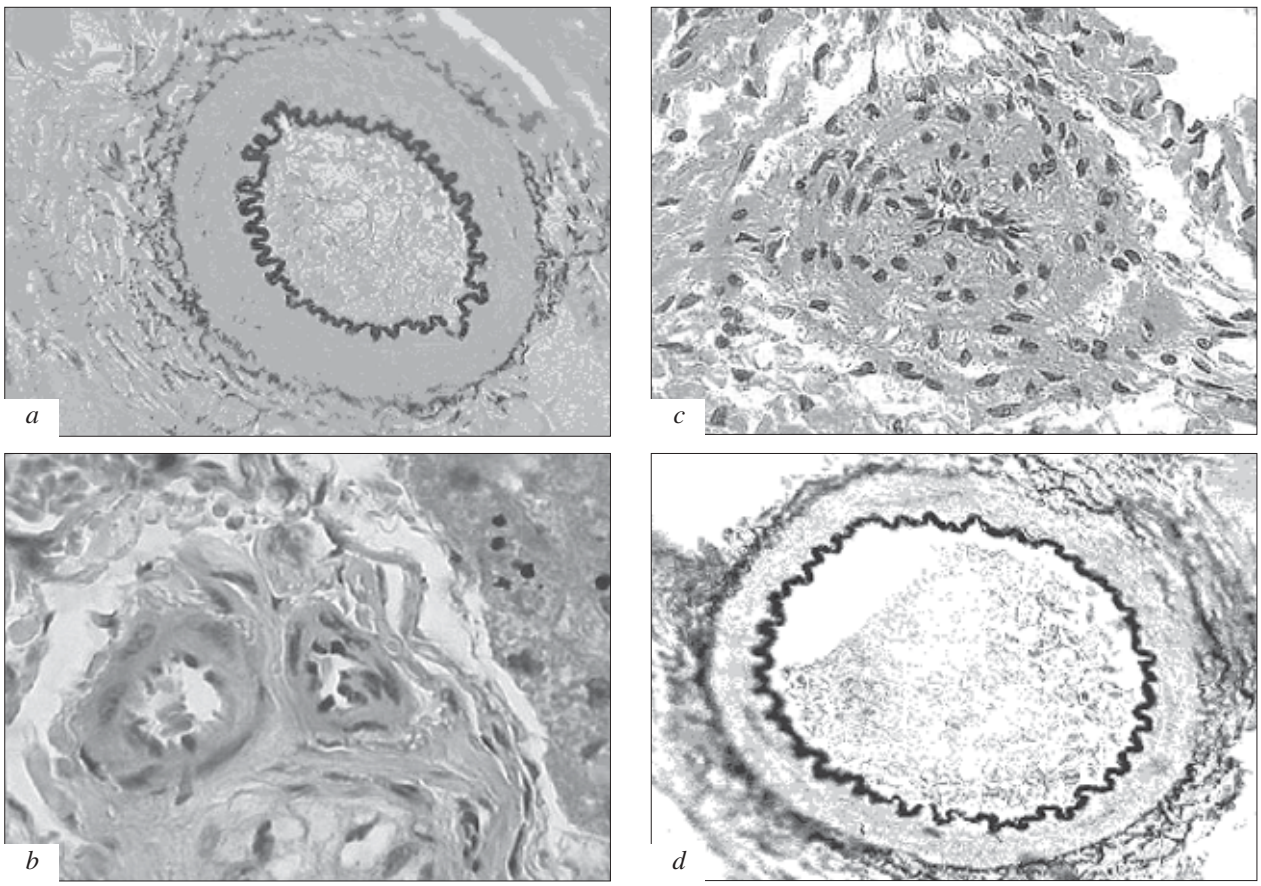

Fig. 1. Hepatic vessels in experimental PTS (*a-c*) and after its elimination (*d*). *a*) thickening of the small arterial wall and increased plication of the inner elastic membrane, ×400, Hart's staining; *b*) bundle of intimal musculature in the wall of a small artery, ×100, hematoxylin and eosin staining; *c*) spasm of medium HV and thickened muscle rolls, ×100, hematoxylin and eosin staining; *d*) thinned wall and decreased plication of the inner elastic membrane in a medium artery, ×400, Hart's staining.

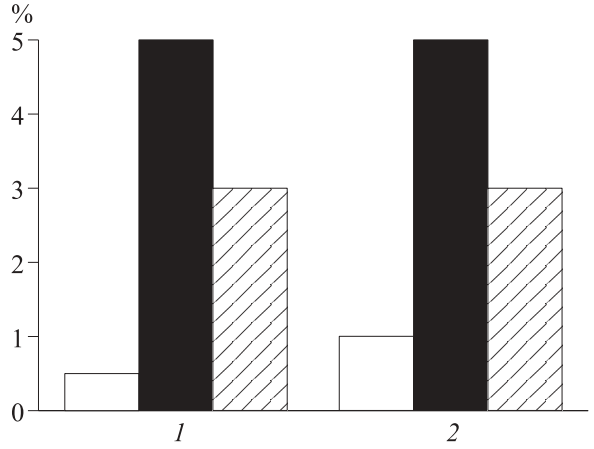

Fig. 2. Prevalence of adaptation structures at the level of small HA in the control (light bars), in PTS (dark bars), and after elimination of PTS (cross-hatched bars). *1*) intimal musculature; *2*) myoelastic sphincters.

Elimination of PTS led to a drop of the HA tone, which was paralleled by dilatation of the arterial lumen, smoothening of the inner elastic membrane, and certain thinning of the media (Fig. 1, *d*). Hypertrophic changes of the walls of portal vein branches also reduced. The number of HA with intimal musculature and sphincters decreased by 1.6 times (Fig. 2). The degree of muscle roll development in the efferent veins visually decreased. Morphometry showed that the thickness of the media in large HA decreased by 1.8 times, in medium and small arteries by 1.2 times, and in arterioles 1.1 times (Table 1). The thickness of the media in afferent veins decreased 1.7 times at the level of large branches, by 1.4 times at the level of medium branches and arterioles, and by 1.6 times at the level of small veins (Table 1). The thickness of the media in large HV drastically decreased (by 5.7 times), in medium veins the media thinned by 2.3 times, and in small veins and venules its thickness decreased by 1.7 times (Table 1). In addition, the mean thickness of the large efferent HV decreased from 50.0±3.4 to 37.0±3.4 μ ($p<0.001$).

Hence, experimental PTS was associated with disturbed blood outflow from the liver with dilatation of HV branches, thickening of their walls, and pronounced hypertrophy of muscle rolls. These rolls play an important role in the compensation for the impaired hepatic circulation, consisting in inhibition of venous congestion [6], threatening for blood circulation in the sinusoidal system, involving subsequent dysfunction of the organ. This was paralleled by reflex contracture of the HA smooth muscles, within the framework of adaptation to a new hemodynamic mode [6,10]. The role of this reflex (veno-arterial reaction) is as follows: the resistance of arteries increases with increasing their tone and later hypertrophy of their walls, which promotes reduction of the sinusoidal hyperemia and protects the microcirculatory system from blood overload. We found that the walls of portal veins, by which the blood is also delivered to the liver, were also subjected to hypertrophic changes. Presumably, this led to reduction of not only arterial, but also of venous blood inflow to this organ (ve-

TABLE 1. Thickness of Hepatic Vessel Tunica Media in the Control, in PTS, and after Its Elimination (μ; *M*±*m*)

Parameter		Control	PTS	PTS elimination
Afferent vessels				
HA	large	24.0±1.1	42.7±2.8*	22.0±1.3^{+}
	medium	13.2±0.8	16.0±0.8*	12.7±0.5^{+}
	small	6.5±0.1	8.1±0.2*	6.5±0.2^{+}
	arterioles	3.70±0.09	3.9±0.1**	3.5±0.2
Portal veins at the levels of				
	large arteries	6.0±0.2	13.9±1.2*	8.0±1.3**$^{+}$
	medium arteries	5.1±0.3	6.9±0.4*	5.0±0.4^{+}
	small arteries	4.1±0.2	5.0±0.2*	3.2±0.1*$^{+}$
	arterioles	2.8±0.1	4.2±0.2**	2.9±0.1^{+}
Efferent vessels				
HV	large	6.2±0.3	31.1±4.1*	5.4±0.6^{+}
	medium	4.4±0.1	9.5±1.1*	4.1±0.2^{+}
	small	3.2±0.1	5.3±0.3*	3.1±0.1^{+}
	venules	2.7±0.1	4.7±0.3*	2.8±0.1^{+}

Note. *$p<0.001$, **$p<0.05$ compared to the control; $^{+}p<0.001$ compared to PTS.

no-venous reaction). Hence, bloodflow resistance increases in afferent vessels, while the possibility for limiting the venous return is created in the efferent vessels. In addition to these compensatory reactions, other adaptation mechanisms are triggered, for example, appearance of specialized regulatory structures, such as bundles of obliquely longitudinal intimal musculature and myoelastic sphincters. The sources of their development are myocytes of the media migrating into the intima through the "windows" in the inner elastic membrane [8]. Due to these contractile structures the bloodflow in the hepatic arterial system is regulated, depending on the blood requirements of various hepatic structural and functional units; that is, despite disturbed hemodynamic mode, the potentialities for blood circulation and adequate tissue metabolism are created [7,11].

Elimination of experimental PTS is associated with improvement of blood outflow from the liver with reduction of functional loading of the HV walls. This is associated with, on the one hand, thinning of previously hypertrophic walls of these vessels with reduction of their muscle rolls and, on the other, the veno-arterial and veno-venous reactions are switched off. This latter event leads to a drop of arterial tone with reduction of the potency of the smooth musculature of the arterial media and reduction of such adaptation structures as the intimal obliquely longitudinal musculature and the myoelastic sphincters, loosing their significance as regulators of local blood circulation. In parallel with this, the walls of intramural portal vein branches are thinned. Hence, elimination of a lasting PTS initiates regression of previously developed structural changes in the hepatic vascular system, which indicates its high plasticity.

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