Reversibility of Changes in Hepatic Vessels after Correction of Experimental Aortic Coarctation

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Structural changes in hepatic vessels were studied in pups with experimental aortic coarctation and animals with corrected defect. Reconstruction of vessels was assayed by functional, morphometric, and histological methods. Aortic coarctation in pups was followed by a decrease in circumferential strain of the wall of hepatic arteries. These changes were accompanied by atrophy and sclerosis of the media. The arterial bed had a greater number of vessels with intimal muscles. Muscle bundles in large hepatic veins underwent dystrophy. After correction of experimental defect, the increase in circumferential strain of arteries was accompanied by hypertrophy of the wall. The number of arterial vessels with intimal muscles decreased, while muscle bundles in hepatic veins were thickened. Sclerosis of hepatic vessels was reversible.

Key Words: *aortic coarctation; reconstruction of hepatic vessels; reversibility*

Aortic coarctation is one of the most common congenital malformations of the cardiovascular system accompanied by severe circulatory disorders [1, 14,15]. Radical surgery for this disease includes excision of the narrowed aortic segment and implantation of a synthetic prosthesis [12]. The outcome of surgical therapy mainly depends on the severity and reversibility of structural changes in vessels of vital organs. Regression of morphological changes in organs and tissues is an urgent problem of biology and medicine [6,7,13].

Here we studied the type of morphological reconstruction in hepatic vessels during experimental aortic coarctation. We evaluated whether morphological changes undergo regression after correction of this disorder.

MATERIALS AND METHODS

Experiments were performed on 25 pups. Experimental aortic coarctation was produced as described elsewhere [6,7]. The animals were examined over 6-12 months. Fifteen pups were killed. In the rest 10 animals the narrowed aortic segment was excised and replaced with a Ftorlon-lavsan prosthesis. These animals were killed after 6-12 months. The material obtained from 10 dogs of similar age served as the control. The animals were killed by bloodletting from the femoral artery under ether anesthesia. The liver samples were taken from various areas and embedded into paraffin. Large (≥125 μ), medium (124-51 μ), and small hepatic arteries (50-21 μ) and arterioles (≤20 μ) were examined after hematoxylin and eosin staining by the method of Masson and Hart. Morphometry of vessels was performed using a screw ocular micrometer. We measured the outer diameter (*D*, without adventitia) and thickness of the media (*m*). The inner diameter was calculated as follows: $d=D-2m$. We estimated the number of small arteries that had bundles of oblique and longitudinal smooth muscles in the intima. Myocytes were counted in the media of these vessels. The size of these cells was determined by the size of nuclei [4,10,11]. The volume and area of their nuclei were calculated as follows: $S=0.785cd$

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and $V=0.523cd^2$, where c and d are the longitudinal and transverse size of the nucleus, respectively. The thickness of muscle bundles was measured at the level of large hepatic veins. Portal inflow pressure was measured with a mercury manometer before killing. This index and morphometric parameters were inserted in the equation: $T=133.3PR/d$, where T is circumferential strain (Pa); P is blood pressure in the vessel (mm Hg); R is the mean radius of arteries (μ); and d is the mean thickness of the wall (μ).The numerical results were analyzed using Statistica software. The differences were significant at $p<0.05$.

RESULTS

Aortic coarctation was followed by a decrease in blood pressure in hepatic arteries from 80 to 50 mm Hg. Arterial tone decreased. The inner elastic membrane of arteries lost rugosity. Circumferential strain decreased by 1.7 times (Fig. 1). We observed an increase in the inner diameter of large and medium arteries (by 1.3 times), small arteries (by 1.4 times), and arterioles (by 1.5 times, Table 1). The media of vessels was thinned. We revealed a decrease in the thickness of the media in large and medium arteries, arterioles (by 1.4 times), and small arteries (by 1.5 times, Table 1). The longitudinal and transverse size of nuclei in smooth muscle cells of these vessels decreased by 1.3 and 1.5 times, respectively ($p<0.001$). The area and volume decreased by 2 and 3.2 times, respectively ($p<0.001$). The number of leiomyocytes in the media decreased by 1.9 times ($p<0.001$). The number of hepatic arteries with intimal smooth muscles increased by 11 times. Arterial muscles were presented by bundles and layers of oblique and longitudinal leiomyocytes

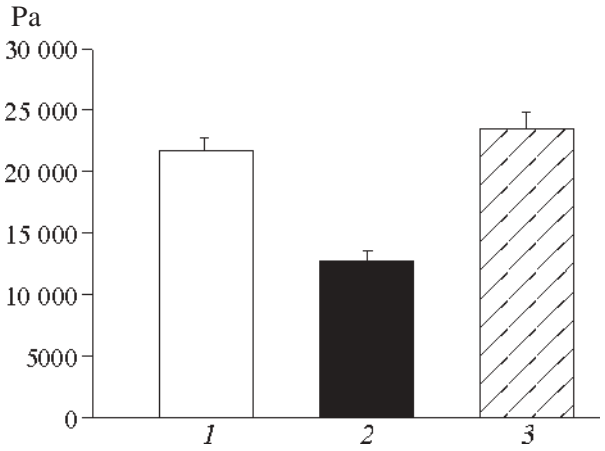

Fig. 1. Circumferential strain under control conditions (*1*), during aortic coarctation (*2*), and after its correction (*3*).

(Fig. 2, *a*). Atrophic changes were also found in large hepatic veins. Morphometry revealed a decrease in the mean thickness of muscle bundles from 36.0±1.5 to 19.0±1.5 μ ($p<0.001$). Sclerotic changes in the hepatic arterial bed became more pronounced, which was manifested in excess growth of connective tissue at the site of atrophic smooth muscle cells (Fig. 2, *b*). Several arteries had a homogenous wall without myocytes (Fig. 2, *c*), which reflected the development of hyalinosis.

Surgical correction of aortic coarctation improved blood inflow in the hepatic vascular bed, which was accompanied by blood pressure rise from 50 to 90 mm Hg. Arterial tone increased, and the inner elastic membrane gained rugosity. These changes were accompanied by a 1.8-fold increase in circumferential strain of vessels (Fig. 1). We observed a 1.3-fold decrease in the inner diameter of large arteries. The inner diameter of medium and small arteries and arterioles decreased by 1.4 times (Table

TABLE 1. Inner Diameter and Thickness of the Wall of Hepatic Arteries during Aortic Coarctation and after Its Correction (μ, $M\pm m$)

Parameter, group	Arteries			Arterioles
	large	medium	small	
Inner diameter				
zcontrol	110.0±2.5	46.8±3.0	16.4±0.4	7.7±0.2
aortic coarctation	141.0±4.4**	62.2±1.4**	24.1±0.9**	11.7±0.3
correction of aortic coarctation	111.0±3.6+	44.0±1.7+	16.6±0.5+	8.5±0.3*+
Thickness of wall				
control	24.08±1.10	13.24±0.88	6.50±0.16	3.84±0.90
aortic coarctation	17.26±0.90**	9.3±0.3**	4.30±0.08**	2.69±0.05**
correction of aortic coarctation	28.0±1.9+	13.1±0.5+	6.50±0.25+	4.14±0.27+

Note. *$p<0.01$ and **$p<0.001$ compared to the control; +$p<0.001$ compared to coarctation.

1). The thickness of the media in large, medium, and small arteries increased by 1.6, 1.4, and 1.5 times, respectively, compared to the aortic coarctation group ($p<0.001$). Hypertrophy of the wall was associated with enlargement of cells in circular muscles. Cell nuclei were elongated and thickened by 1.5 times ($p<0.001$). The area and volume of these structures increased by 2.2 and 3.2 times, respectively ($p<0.001$). The number of myocytes in the media increased by 1.9 times ($p<0.001$). The number of inflow vessels with oblique and longitudinal muscles decreased by 5 times. Hepatic veins were characterized by hypertrophy of strongly contracted smooth muscle bundles (Fig. 2, *d*). Morphometry revealed an increase in the thickness above the control level (from 19.0±1.5 to 49.0±2.7 μ, $p<0.001$). The severity of sclerotic changes in various arteries decreased under these conditions.

Our results show that experimental aortic coarctation and decrease in portal inflow pressure are followed by reactive relaxation of the arterial wall and reduction of circumferential strain. The decrease in functional load of vessels leads to atrophy of leiomyocytes and, therefore, thinning of the wall. Intimal muscles become more developed in hepatic inflow vessels. Published data show that these muscles play a role in the regulation of blood flow in organs [2,8-10]. These changes are accompanied by thinning of muscle bundles in hepatic veins that provide blood stagnation in hepatic vessels [2,3,5,11]. Biologically, atrophy eliminates the necessity for accumulation of venous blood. The changes observed under conditions of coarctation occur due to hypotension in the systemic circulation. Reserve blood is mobilized from the liver to compensate chronic ischemia in organs and tissues. Vascular sclerosis and hyalinosis in atrophic hepatic vessels develop in the follow-up period.

Correction of experimental defect improved blood supply to the liver, increased arterial tone and circumferential strain of the arterial wall. Increased functional load contributes to thickening of the wall of these vessels, which is associated with hypertrophy and hyperplasia of circular muscles in the media. However, oblique and longitudinal muscles in hepatic arteries lose the ability to regulate local blood circulation. These muscles become less developed after corrective surgery. Surgical correction of coarctation is accompanied by normalization of blood pressure in systemic circulation. Blood stagnation in hepatic veins results in hypertrophy of muscle bundles. These veins can accumulate a greater amount of blood. The organs exposed to long-term hypotension do not necessitate the in-

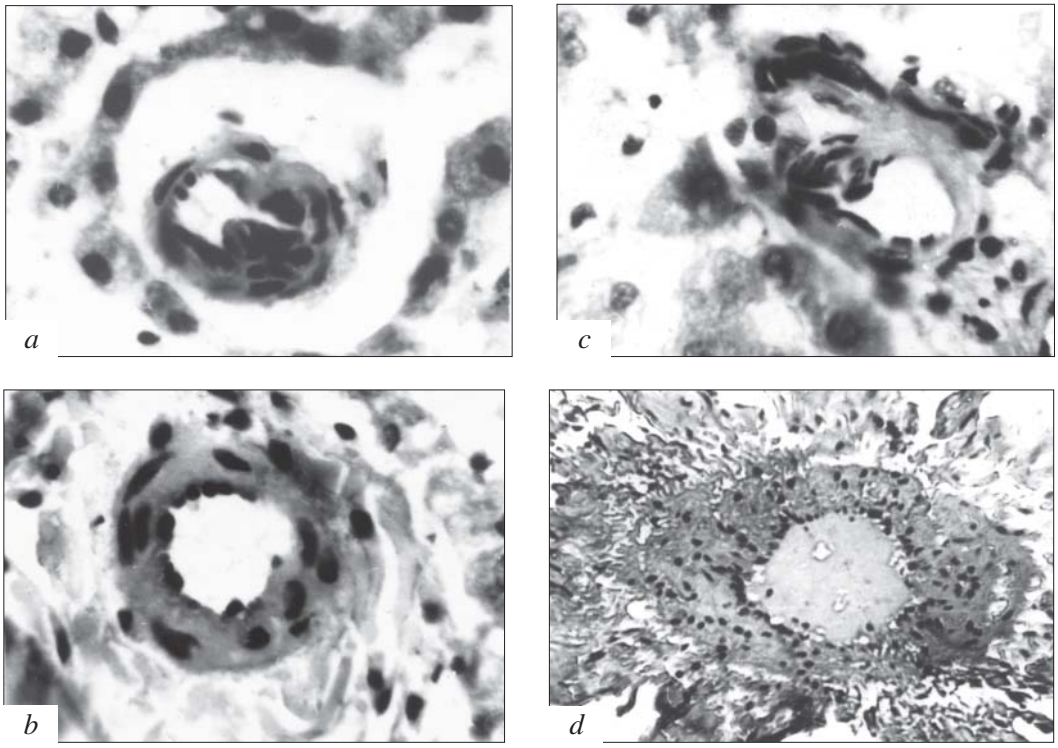

Fig. 2. Hepatic vessels during experimental aortic coarctation (*a-c*) and after its correction (*d*). (*a*) Bundle of intimal muscles in a small artery; (*b*) sclerosis of the wall in a small artery; (*c*) hyalinosis of the wall in a small artery with muscle bundle. (*a-c*) Hematoxylin and eosin staining, ×400. (*d*) Hypertrophy of muscle bundles in the wall of the hepatic vein. Masson's staining, ×160.

creased inflow of blood after restoration of blood flow. Therefore, considerable amounts of blood are accumulated in the liver. The signs of recovery concern not only atrophic, but also sclerotic hepatic arteries. Our results indicate that correction of prolonged aortic coarctation contributes to regression of changes in hepatic vessels. These data reflect high plastic capacity of the liver.

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