Possible Reversibility of Structural Changes in Renal Vascular Bed after Correction of Experimental Coarctation of the Aorta

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 142, No. 9, pp. 346-349, September, 2006
Original article submitted December 19, 2005

Renal vessels were studied in 22 puppies with induced coarctation of the aorta, 15 with corrected defect, and 12 controls by functional, histological, and morphometrical methods. Constriction of the isthmus of the aorta was associated with decreased pressure of blood flowing to the kidneys and pronounced morphological restructuring of the renal blood system components. Correction of the experimental defect triggers the mechanism of regression of previously induced changes and promotes appreciable recovery of the structure of renal arteries, veins, and glomeruli.

Key Words: *coarctation of the aorta; renal vascular system; reversible structural changes*

Coarctation of the aorta is a prevalent congenital disease to be treated surgically [4,12]. The efficiency of the operation is determined not only by surgeon' professional skills, but also by the degree of reversibility of vascular system changes in vital organs, *e.g.* the kidneys [9]. Evaluation of the recovery of the structure of various components of local blood flow after correction of coarctation suggests studies of the kidney as a whole organ, which can be done under experimental conditions.

We studied the specific features of restructuring of various compartments of the renal vascular system in simulated coarctation of the aorta and investigated the possibility of their regression after correction of the defect.

MATERIALS AND METHODS

Experimental defect was induced in 37 puppies [8]; in 15 of these it was corrected (constricted part of the aorta was resected and replaced with a vascular prosthesis). Both groups of animals were observed for 6 months to 2 years. The pressure of blood flowing to the kidneys was measured by manometry. Control group consisted of 12 age-matched dogs.

The animals were sacrificed by bleeding under narcosis. Fragments of the kidneys were fixed in 10% neutral formalin and embedded in paraffin. The preparations were stained by hematoxylin and eosin, after Van Gieson and Hart. Quantitative evaluation of arteries, veins, and capillary glomeruli was also carried out by stereometry (point count method [1]) and their specific area was determined. Morphometry was carried out using a screw ocular micrometer. The external (D) and inner (d) diameters of interlobar (ILA), arch (AA), and interlobular (ILLA) arteries and arterioles were measured. The thickness of the wall and transverse section areas of these vessels were evaluated by the formulas: $m=(D-d)/2$ and $S=pm(D-m)$ [1]. The content of smooth muscle cells in the ILLA tunica media was evaluated; their size was evaluated by the size of their nuclei [2]. The nuclear volume was estimated by the formula: $V=0.523cb^2$ [1], where c

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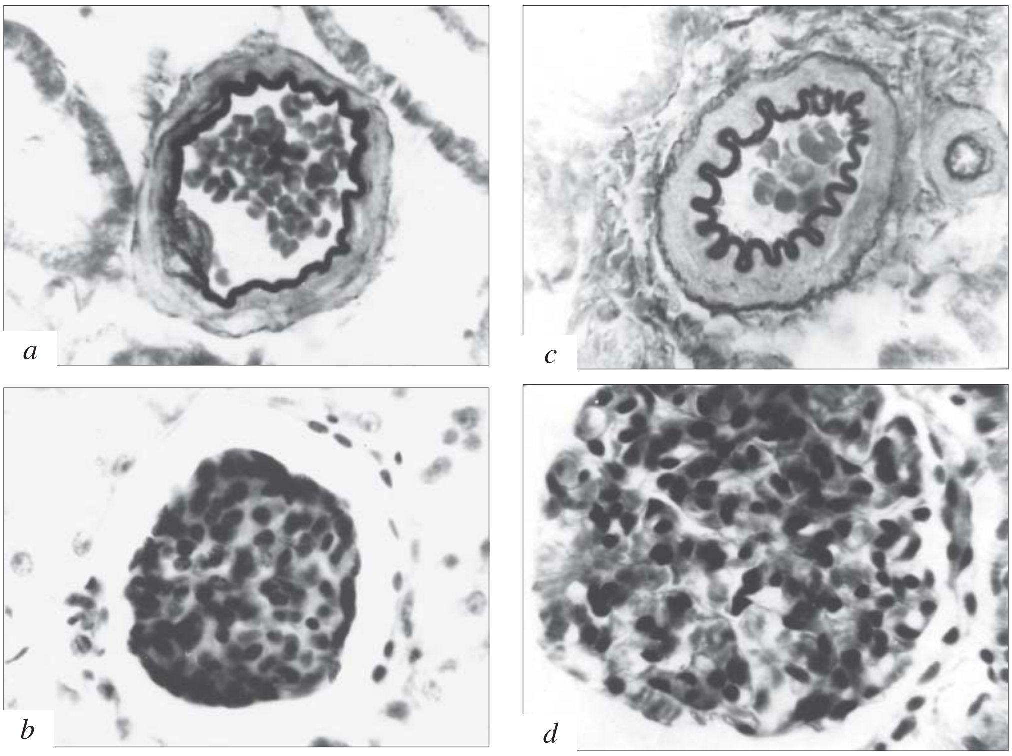

Fig. 1. Status of various components of the dog renal vascular system in experimental coarctation of aorta (*a*, *b*) and after its correction (*c*, *d*). *a*) uneven thickness and plicated inner elastic membrane of interlobular artery after 12 months; *b*) ischemic capillary loops and renal glomerulus collapse after 6 months; *c*) restoration of even thickness and plication of inner elastic membrane of interlobular artery after 10 months; *d*) restoration of blood content of capillary loops and increase in the renal glomerulus size after 6 months; *a*, *c*) staining after Hart (×400); *b*, *d*) hematoxylin and eosin staining (×400).

and b are the maximum and minimum diameters of the nucleus. The percentage of arteries of different levels of branching with obliquely and longitudinally oriented smooth myocytes in the intima was evaluated. The thickness of renal vein walls was determined as the quotient of division of the sizes of the thinnest and thickest parts of these vessels. The status of the glomeruli was objectively evaluated by counting them in a microscope visual field (at ×80) in the median zone of the renal cortical layer and by measuring the diameter of these formations and counting the cells on their transverse section. The numerical data were processed by methods of variation statistics.

RESULTS

Constriction of the isthmus of the aorta led to pressure drop in the blood flowing to the kidneys from 85±0 to 50±0 mm Hg ($p<0.05$) and was associated with the development of hypotension of the organ arteries, which was seen from uneven plication and thinning and sometimes cleavage of their internal elastic membrane (Fig. 1, a). Blood content of these vessels decreased, which was paralleled by a decrease of their specific area (1.6 times; Fig. 2). Sclerotic changed developed in some renal arteries. The transverse section area decreased 1.9 times in ILA, 1.2 times in AA, 1.8 times in ILLA, and 1.5 times in arterioles (Table 1). Smooth-muscle cell nuclei volume in ILLA tunica media decreased from 67.8±1.8 to 31.2±2.1 μ^3 ($p<0.001$), the count of these cells decreased from 11.9±0.2 to 8.2±0.2 ($p<0.001$). On the other hand, the percentage of vessels with bundles of obliquely and longitu-

TABLE 1. Area of Renal Arteries Transverse Section in Dogs with Experimental Coarctation of Aorta (μ^2; $M\pm m$)

Parameter	Control	Coarctation of aorta	Correction of coarctation of aorta
ILA	27150±564	17800±300***	25076±430*+
AA	5620±168	4623±75***	5208±90*+
ILLA	2012±58	1147±22***	1680±28***+
Arterioles	420±15	283±9***	360±14**+

Note. *$p<0.05$, **$p<0.01$, ***$p<0.001$compared to the control, +$p<0.001$ compared to the corresponding value in coarctation of the aorta.

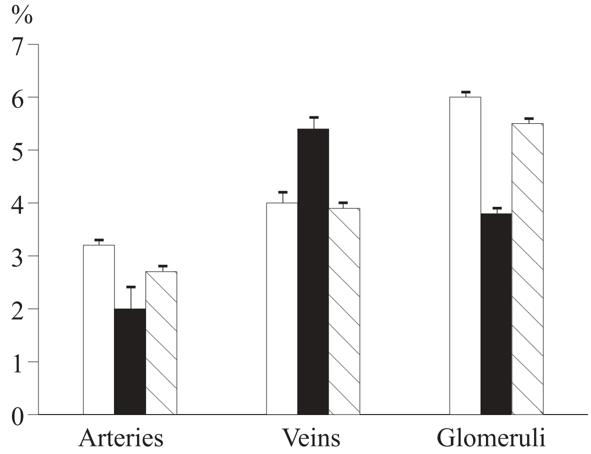

Fig. 2. Specific area of renal arteries, veins, and glomeruli in dogs with experimental coarctation of the aorta. Light bars: control; dark bars: coarctation of aorta; cross-hatched bars: repair of coarctation of aorta.

dinally oriented smooth muscle cells in the intima increased among the renal basin arteries. The number of these vessels at the level of AA increased from 2.3 to 10.0%, at the level of ILLA from 2.5 to 17%. Among arterioles 9.5% vessels of this kind were detected.

Blood content of renal veins increased, which led to increase in their specific area (1.4 times; Fig. 2). The walls of these vessels thickened from 3.0±0.5 to 6±1 μ (p<0.001).

Renal glomeruli were characterized by ischemia of capillary loops. Collapsed (Fig. 1, *b*) and sclerosed glomeruli were seen. Their specific area decreased 1.6 times (Fig. 2). The number of glomeruli in a microscope visual field increased 1.2 times, while their diameter and number of cells per section area decreased 1.2 times (Table 2).

Surgical correction of experimental coarctation of the aorta was associated with a pressure increase in the renal basin blood (to 90±10 mm Hg). This

TABLE 2. Renal Glomeruli in Dogs with Experimental Coarctation of the Aorta (*M*±*m*)

Parameter	Control	Coarctation of aorta	Correction of coarctation of aorta
Number of glomeruli	12.2±0.2	14.4±0.3*	12.3±0.2*
Diameter of glomeruli, μ	103.4±0.6	85.9±0.7*	101.7±0.3*+
Number of cells in glomeruli	131.4±0.9	112.8±0.6*	130.6±0.3*

Note. *p<0.001 compared to the control; +p<0.01 compared to the corresponding parameter in coarctation of the aorta.

was paralleled by an increase in the arterial tone, the internal elastic membrane of arteries acquiring an even thickness and common plication (Fig. 1, *c*). Blood content of these vessels increased, their specific area increased 1.3 times (Fig. 2). Signs of sclerotic changes were rarer and less pronounced. Arterial walls thickened, which led to an increase in their section area 1.4 times for ILA, 1.1, 1.5, and 1.3 times for AA, ILLA, and arterioles, respectively (Table 1). The volume of smooth-muscle cell nuclei in ILLA tunica media increased to 47.4±2.2 μ^3 (p<0.001). The count of myocytes in this vascular membrane increased to 9.8±0.2 (p<0.001). The number of arteries containing obliquely and longitudinally oriented smooth muscle cells in the intima also changed after correction of the coarctation: their number decreased to 6.6% among AA, to 9.2% among ILLA, and to 6.1% at the level of arterioles.

Renal vein blood content virtually normalized after correction, the specific area of these vessels decreased 1.4 times (Fig. 2) and the thickness of their walls reached 3.4±0.6 μ (p<0.05).

Capillary loops of the glomeruli became more plethoric in animals with corrected coarctation (Fig. 1, *d*). Shrunk and sclerosed glomeruli were rare. The mean specific area of these formations increased 1.4 times (Fig. 2), their content per standard area decreased 1.2 times, while the diameter and count of the cells increased 1.2 times (Table 2).

We found that creation of the aortic coarctation model was associated with impairment of renal blood supply with an appreciable reduction of the capacity of the arterial compartment of their vascular basin. Decrease in the hemodynamic loading of the renal arterial branches led to degeneration of the circular muscles in tunica media of these vessels and to a decrease in transverse section area of their walls. These changes are reactive and adaptive. The decrease in the pressure of blood flowing to the kidneys is fraught with disorders in glomerular filtration. Adaptation of the renal arterial bed to the new hemodynamic situation results in an increase in the number of vessels with bundles of obliquely and longitudinally oriented smooth muscle cells in the intima. According to published data [7,10,13], they migrate here from the media, penetrating through the "windows" in the elastic membrane. This migration is a result of the universal reaction of the vascular wall to extreme, including hemodynamic, factors [11]. The lumen of thus restructured arteries can drastically constrict, because of which they were called closing. They can regulate the volume of blood flowing in them, thus providing blood saturation of the functioning glomeruli, needed for renal work. The increase in the renal vein capacity also maintains the glomerular hemocirculation homeostasis. This is most probably due to blood deposition in this compartment of the renal vascular system, which leads to deceleration of its movement via the capillary system of the glomeruli and improves the conditions for their functioning. Involvement of the arterial and venous mechanisms maintains the glomerular filtration at the adequate level even in case of pronounced pressure reduction in the renal basin.

With time pathological changes emerge and progress in the renal vascular system against the background of adaptation processes. Renal arterial walls are sclerosed, which causes impairment of the renal glomeruli perfusion with collapse, degeneration, and sclerosis of some structures.

Correction of artificially created coarctation leads to recovery of pressure of the blood flowing to the kidneys and stimulates the regression of functional and morphological changes in their vessels. Renal arterial tone increases, blood content of their branches appreciably improves. Increase of the functional loading of these vessels is associated with hypertrophic hyperplastic changes in the circular musculature of the tunica media, which leads to thickening of arterial walls and promotes resorption of collagen by myocytes [5] and their enzymes [6,14] with reduction of sclerosis manifestations. Under conditions of normalization of the blood flow to the kidneys, no well-developed system for the blood flow regulation is needed any longer, and the number of arteries reconstructed by the closing type is decreased. This is paralleled by cessation of blood deposition in the renal venous collectors, and their capacity is restored and the walls are thinned. All this improves the hemocirculation at the level of the glomeruli: they increase in size, the intensity of degenerative and sclerotic changes decreases.

Hence, surgical correction of coarctation of aorta arrests the adaptation and pathological restructuring of the renal blood system and stimulates reparative changes, though no complete restoration of the vascular system of these organs was observed during the period of observation (6 months to 2 years) in this study.

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