MORPHOLOGY AND PATHOMORPHOLOGY

Morphofunctional Changes in the Intima of Collateral Arteries in Modeled Aorta Coarctation

S. G. Chasovskikh, L. M. Nepomnyashchikh, G. M. Kazanskaya, I. I. Semenov, amd G. G. Chasovskikh

UDC 616.127-018.1-02:612.275.1]-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 7, pp. 82-85, July, 1994
Original article submitted April 4, 1994

In modeled aorta coarctation long-term functioning of collateral arteries is shown to be accompanied by activation of subintimal smooth muscle cells and elastofibrosis of the intima, which are a manifestation of hemodynamic arteriosclerosis.

Key Words: *aorta coarctation; compensation; electron microscopy; radioautography*

In the development of compensatory processes in response to hemodynamic disturbances in heart defects an important role is played by not only cardiac but also extracardial (vascular) mechanisms [2-4]. Among the various cardiovascular defects aorta coarctation occupies a prominent place, being the only natural model which is characterized by the simultaneous presence of hyper- and hypotensive zones in the organism. These zones form after critical narrowing of the magistral flow is attained [7], the leading mechanism of extracardial compensation being the development of the collateral circulation [1]. However, morphological changes in collateral arteries in this heart defect have not been studied, especially with current methods.

The objective of the present study was a morphofunctional investigation of the dynamics of early hemodynamic rearrangement of the intima of collateral arteries in experimental aorta coarctation.

Institute of Regional Pathology, Siberian Division of the Russian Academy of Medical Sciences; Research Institute of Circulation Pathology, Ministry of Health of the Russian Rederation, Novosibirsk. (Presented by L. D. Sidorova, Member of the Russsian Academy of Medical Sciences)

MATERIALS AND METHODS

The isthmus of the aorta was one-third narrowed by silk ligature in 85 2-month-old nonpedigree puppies. Twenty-eight dogs died immediately after surgery and 6 intact one-year-old animals served as controls. The 57 survivors were divided into 3 groups according to the time of development of aorta coarctation: 2-4 months (11 observations) up to 9-11 months (4 observations) and 14 months (6 observations). Biopsy material was collected from the wall of collateral vessels (the intercostal and thoracic arteries) above and below the narrowing of the aorta. All samples were embedded in paraffin and stained with hematoxylin-eosin and after van Gieson, followed by additional staining of elastic tissues with resorcin-fuchsin. In some cases the samples were examined by transmission (23 experimental and 4 control samples) and scanning (13 and 6 samples, respectively), microscopy and by radioautography of semithin sections stained with methylene blue and azure 2 (17 and 4 samples, respectively).

RESULTS

As the animals grew, the coarctation of the aorta increased and after 6 months the lumen was 1/2

0007-4888/94/0007-0767$12.50

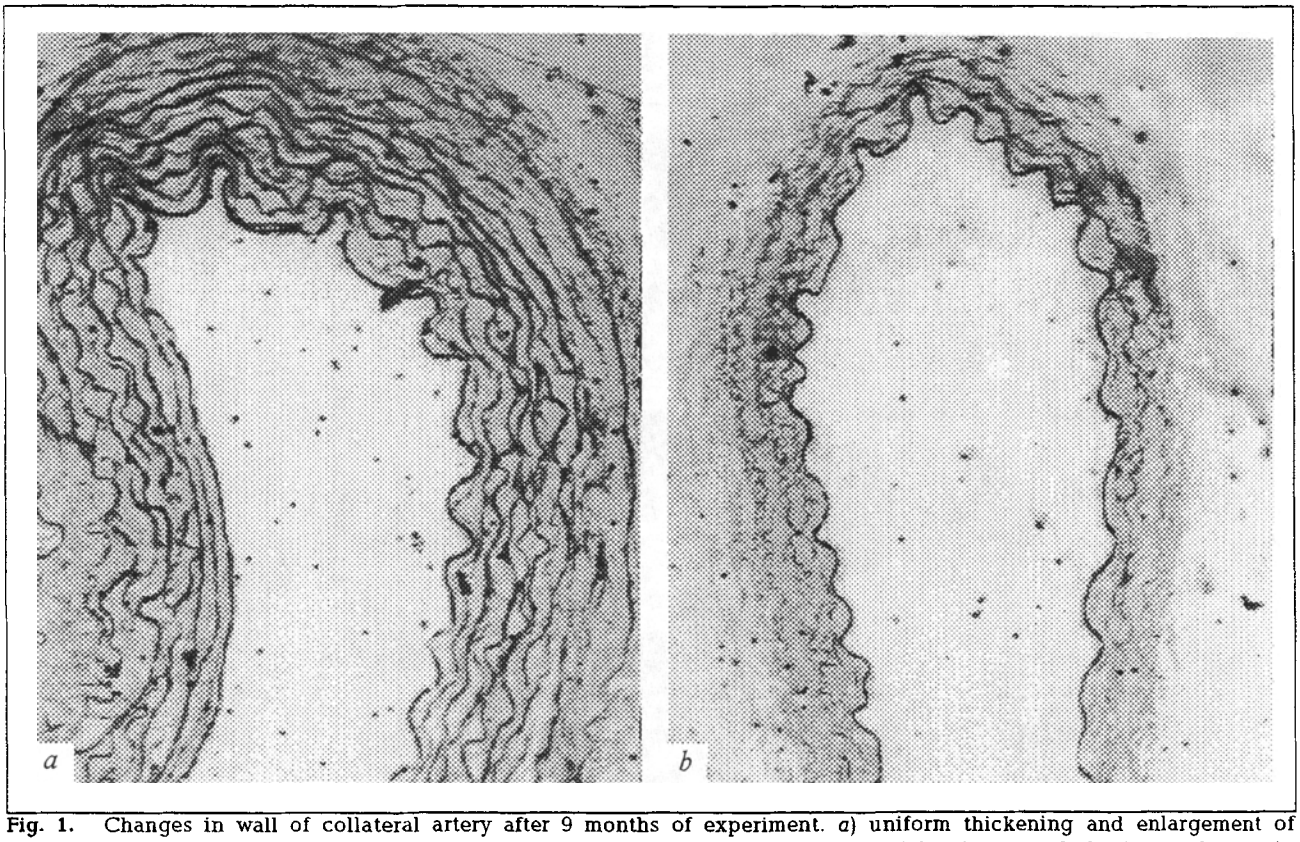

Fig. 1. Changes in wall of collateral artery after 9 months of experiment. *a*) uniform thickening and enlargement of elastic layers in the media of a proximal collateral; *b*) thinning of arterial wall, partial reduction of elastic membranes in the middle layer of a distal collateral. Semithin section, methylene blue and azure 2 staining, ×200.

and after one year 1/3 of the diameter above and below the narrowing. The pressure gradient was 23±5 in 2-4 and 9-11-month-old animals and 25±5 in one-year-old animals, the systolic pressure in the control group being 100 mm Hg.

On histological specimens and semithin sections of the wall of collateral arteries above the coarctation a thickening of the middle layer and of the internal and other elastic membranes of the vessel were noted (Fig. 1, *a*), while below the coarctation previously fibrous contours of elastic membranes were smoothed and then (by the 7th month of the experiment) underwent atrophic thinning or partial reduction (Fig. 1, *b*).

Scanning electron microscopy of proximal collateral arteries revealed partially preserved intima folds directed along the axis of the blood flow. However, at later stages of the experiment they looked more irregular and rough, and in some regions we observed randomly interlaced folds. Recesses at sites of transverse interruptions of longitudinal folds of the inner elastic membrane were more common in this layer of the vascular wall in comparison with the control. The bottom of such "pits" showed an increased number of endotheliocytes (Fig. 2, *a*).

Sites of older alterations of the inner elastic membrane were characterized by foci of pathological regeneration of elastic structures presenting as malformed folds, connected with cross-pieces and and with no unified direction (Fig. 2, *b*).

In the distal regions of collateral arteries the intima was often smoothed (Fig. 2, *c*), the remaining folds looked thin and some were no

TABLE 1. Index of ^{3}H−Uridine Labeling in Endotheliocytes of Collateral Arteries in Experimental Aorta Coarctation (% of Examined Cells)

Time of experiment	Above coarctation		Below coarctation	
	^{3}H-uridine	^{3}H-thymidine	^{3}H-uridine	^{3}H-thymidine
Control	35.75±7.1	–	–	–
2–4 months	53.3±6.3	0.42±0.03	35.4±8.0	0.08±0.011
9–11 months	73.2±3.4	0.175±0.019	56.0±5.9	0.133±0.014
14 months	86.0±5.9	0.15±0.016	40.8±3.4	0.07±0.015

longer strictly directed along the blood flow. We also observed transverse interruptions of the longitudinal folds of the inner elastic membrane and more densely packed nuclei of endotheliocytes on the bottom of the formed pits (Fig. 2, *d*). This portion of collateral vessels was characterized by endotheliocyte desquamation and partial loss of cell-cell contacts.

Transmission electron microscopy revealed stellate cells entering from the subintimal portion of the smooth muscle layer of the vascular wall (Fig. 3, *a, b*). In some cases their processes attained sites with no contacts between endotheliocytes. Expansion of the processes and in some cases migration of the cells toward the endotheliocyte monolayer occurred through gaps in the now fragmentary inner elastic membrane. Cytoplasmic processes of endotheliocytes toward smooth muscle cells were less abundant.

Radioautography revealed incorporation of ^{3}H-uridine and ^{3}H-thymidine into the endothelial monolayer of collateral arteries and among the subintimal smooth muscle cells. The index of ^{3}H-uridine incorporation rose in all experimental groups in comparison with the control and over the entire experimental period (Table 1). This ten-

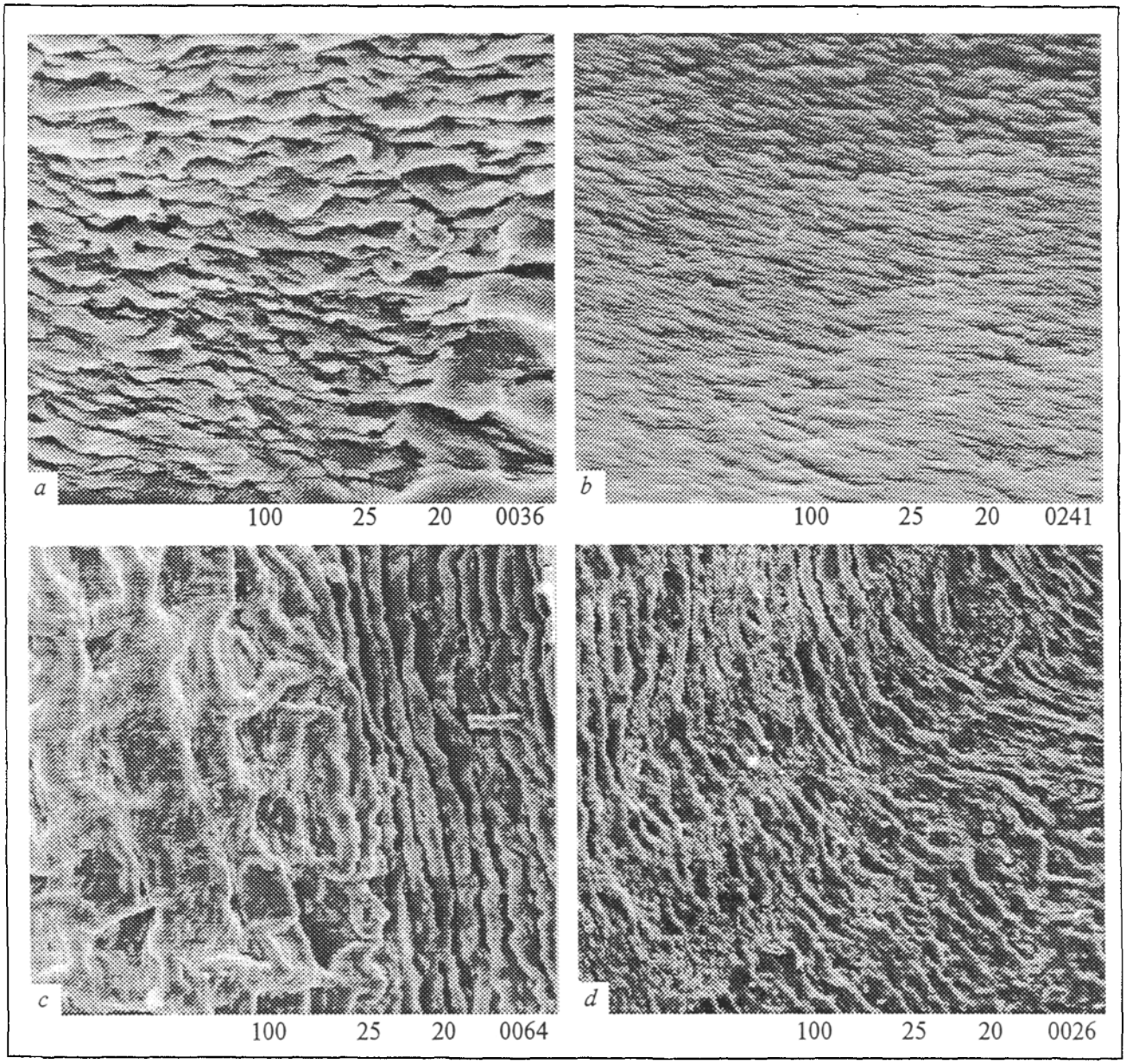

Fig. 2. Changes in the intima profile of a collateral artery. *a*) dense monolayer of endotheliocytes and longitudinal folds in recess at site of intima rupture; *b*) coarse tangle of pathologically thickened structures of inner elastic membrane at site of intima rupture of a proximal collateral; *c*) smoothed profile of lumen of a distal collateral; *d*) multiple defects of folds with denser arrangement of cells in intima of a distal collateral. Scanning electron microscopy.

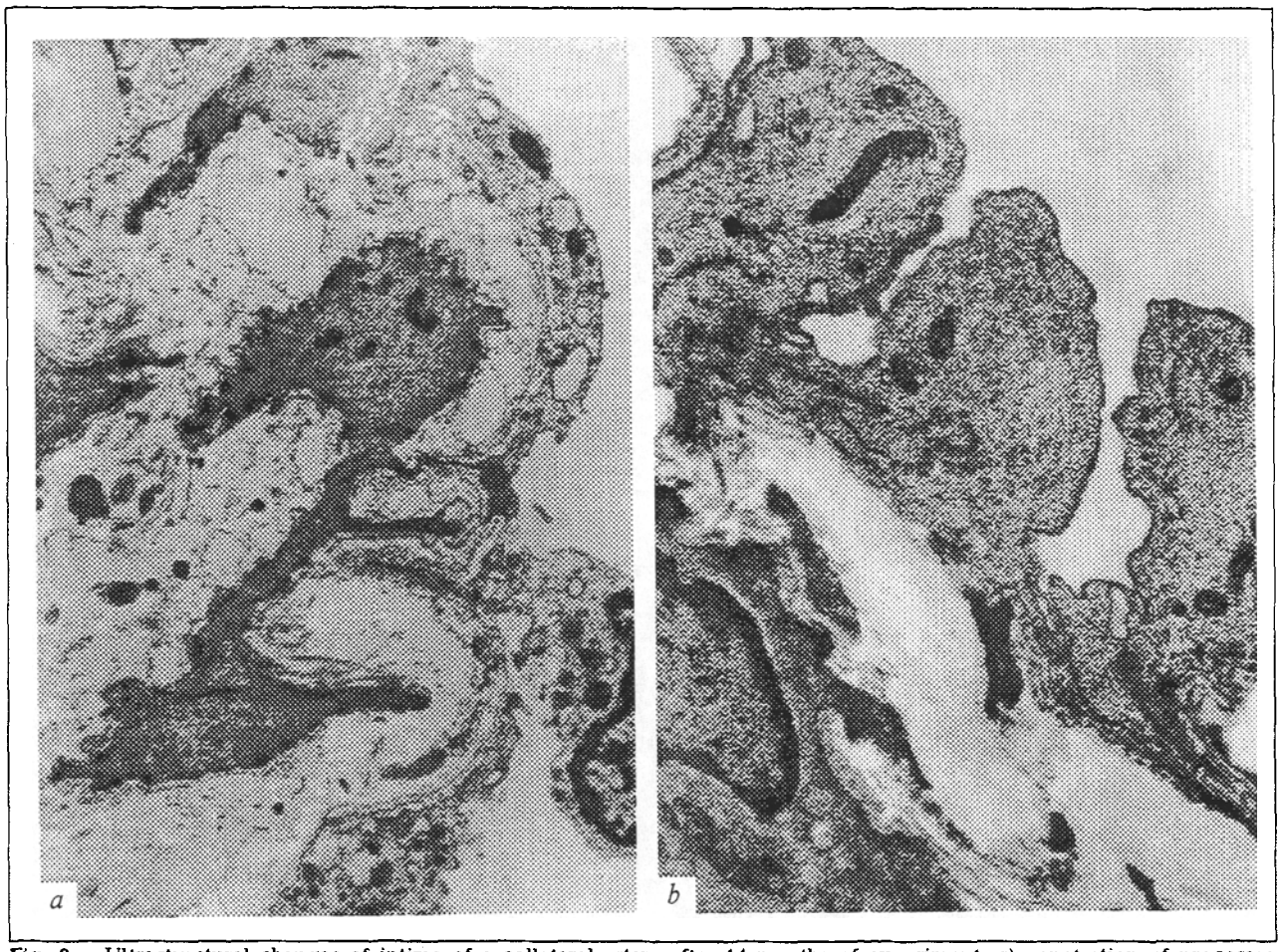

Fig. 3. Ultrastructural changes of intima of a collateral artery after 14 months of experiment. *a*) penetration of processes of subintimal smooth muscle cells through defects of inner elastic membrane toward endotheliocyte monolayer, ×8750; *b*) endotheliocytes exposed to the lumen, fragment of broken inner elastic membrane, and stellate subintimal smooth muscle cell. Transmission electron microscopy.

dency was noted in arteries above and below the coarctation but in the former it was 1.5-2-fold more pronounced. The above changes were somewhat better expressed in the proximal than in the distal portion of the collateral vessels.

The combined study of early changes in the inner layer of collateral arteries in modeled aorta coarctation pointed up the initial mechanisms of vascular hemodynamic rearrangement. The elevated pressure above the narrowing and lowered pressure below it in such arteries result in a compensatory angiospastic effect in the hypertensive zone and decreased vascular tonus in the hypotensive zone, which is accompanied by progressive dilatation of the lumen, stretching of the vascular wall, and atrophy of its elastic and muscular structures.

Scanning electron microscopy demonstrated that these changes result in damage of the endothelial monolayer, partial dystrophy of cells, ruptures of the inner elastic membrane, and destructive changes of the basal membrane. This is followed by repair of the destroyed sites with regenerative hyperplasia of endotheliocytes and progressive restoration of the basal membrane [10].

Transmission electron microscopy showed that the adjacent layer of smooth muscle cells participates actively in regeneration of the intima.

Radioautography demonstrated an activation of metabolic processes in these cells [9]. The involvement of subintimal cells into regeneration is evidently a natural phenomenon.

There are published data [5,8] on a close interrelationship between endotheliocytes and subintimal smooth muscle cells and activated synthesis and secretion of proelastin and procollagen in the latter in response to the breakdown of cell-cell contacts. The hyperproduction of paraplastic substances together with delayed regeneration of the endothelial monolayer evidently results in pathological elastomuscular thickenings at the sites of intima defects, which are clearly seen in the later stages of regeneration upon histological examination of the intima of collateral arteries in patients with aorta coarctation [6]. This mechanism evidently

illustrates the early stages of arteriosclerosis which are also characteristic for other types of sclerosis of the vascular wall.

REFERENCES

1. N. A. Belokon' and V. P. Podzolkov, *Congenital Heart Defects* [in Russian], Moscow (1991).
2. I. K. Esipova, *Notes on the Hemodynamic Rearrangement of the Vascular Wall* [in Russian], Moscow (1971).
3. E. N. Meshalkin, E. E. Litasova, and Yu. A. Vlasov, in: *Cardiosurgery and Cardiological Problems with Respect to the Dynamics of Compensation-Paracompensation in Heart Defects* [in Russian], Novosibirsk (1990), pp. 3-14.
4. Painter, Hines, and Edwards, *Problems of the Cardiovascular System*, № 3, 63-78 (1953).
5. M. D. Rekhter, V. A. Kolpakov, and A. A. Mironov, *Arkh. Patol.*, № 1, 65-68 (1992).
6. I. I. Semenov, S. G. Chasovskikh, *et al.*, in: *Clinical, Structural, and Physiological Aspects of Cardiosurgical Pathology* [in Russian], Novosibirsk (1992), pp. 239-249.
7. G. M. Solov'ev and Yu. A. Khrimlyan, *Aorta Coarctation* [in Russian], Erevan (1968).
8. H. Beheendt and W. Kuhneb, *Virch. Arch*, **20**, № 4, 347-350 (1976).
9. R. Bevan, *Blood Vessels*, **13**, № 1-2, 100-128 (1971).
10. H. Masuda, K. Kawamura, K. Tohda, *et al.*, *Role of Blood Flow in Atherogenesis: Proc. Int. Symp.* (Hyodo, Oct. 1987), Tokyo (1988), pp. 163-169.

Changes in the Blood-Brain Barrier in Experimental Cirrhosis of the Liver

V. A. Mishchenko, O. A. Goryukhina, and R. D. Ilyuk

UDC 616.831-002:616.36-004

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 7, pp. 86-88, July, 1994
Original article submitted December 12, 1993

Light and electron microscopic studies on Wistar rats with experimental cirrhosis produced by tetrachloromethane demonstrate strongly marked changes in the blood-brain barrier, particularly in capillaries and vascular pedicles of astrocytes. It is pointed out that destabilization of the blood-brain barrier favors the transfer of cerebral toxins and other metabolic poisons across this barrier.

Key Words: *blood-brain barrier; experimental cirrhosis*

The state of the blood-brain barrier (BBB) is of great importance for the functioning of the nervous system and of the body as a whole. The BBB is thought to be composed of perivascular processes and capillaries that include the endothelium and the basement membrane with pericytes and mast cells closely associated with the latter [9]. It has been suggested that pericytes may be involved in providing what is called "motor innervation" of the capillaries and in the transfer by them of information on alterations in the metabolic environment; as a result, the endothelial cells of brain capillaries begin responding to biologically active substances such as histamine, serotonin, and others [13]. According to some authorities, pericytes can also produce an intermediate substance and perform a barrier function by exhibiting phagocytic activity [8].

It has been stated recently that the BBB should also be considered to include tissue basophils (mast cells) with organic features characteristic of the nervous system [5]. The perivascular processes of astrocytes are believed to be responsible for as much as 85% of the control exercised

Department of Nervous Diseases with a Course in Neurosurgery, Medical Institute of Sanitation and Hygiene, St. Petersburg (Presented by I. P. Ashmarin, Member of the Russian Academy of Medical Sciences)

0007-4888/94/0007-0771$12.50