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Features of angioarchitectonics and morphological structure of the vessels of the brachiocephalic trunk in patients with aortic arch hypoplasia

Abstract

Aim: Make a comparative assessment of structural changes of the left subclavian artery in case of hypoplasia of the aortic arch in children of the first year of life..

Material and Methods: In the study were included 35 patients, with hypoplasia of the aortic arch, operated in the central pediatric surgery НИИИПК named. akad. E.H. Meshalkin during 2013-2015 years. Inclusion criteria: age 65.4 ± 83.9 days (from 1 to 281 days), average body weight 3.3 ± 1.05 (from 1.85 to 6.4 kg), All patients underwent surgical correction of congenital heart disease (CHD) - hypoplasia of the aortic arch with a modified reverse flap plasty left subclavian artery under normothermic conditions. Biomaterial was taken intraoperatively: a fragment of the subclavian artery for the study of angioarchitectonics, proportions of elastin and collagen fibers, also changes there proportions in the wall of the intact subclavian artery and of the subclavian artery of the patients with hypoplasia of the aortic arch. The control group consisted of patient at the same age, who died after surgery for other congenital heart defects (n=27).

Results: Comparative analysis revealed that the content of thin collagen fibers in patients of control group (normal subclavian artery) was significantly less, than in patients of this study. Also revealed the predominance elastin fibers in patients with pathologically unchanged subclavian artery, than in coarctation zone.

Conclusion: Structural changes in the vessels of the brachiocephalic trunk (subclavian artery) as CHD, hypoplasia of the aortic arch in children of the first year of life, characterized by a predominance of the number of collagen fibers over the number of elastin fibers. These changes associated with the proliferation of smooth myocytes, myofibroblasts and fibroblasts (changes of proportions between cell types). These structural changes able to decrease elasticity, resulting in the development of hemodynamic disorders.

Keywords: Hypoplasia of the aortic arch, morphology, elasticity

INTRODUCTION

Aortic coarctation belongs to the group of common anomalies among congenital heart defects (CHD). The prevalence of this defect among newborns and infants consist for 6-10% of cases (1). At the same time, in 70% of the cases segmental narrowing of the aorta associated with hypoplasia distal or whole aortic arch. From the end of the 20th century in cardiovascular surgery is discussed the pathogenetic role of aortic arch hypoplasia as one of the leading pathogenetic factors in the formation of long-term complications (cerebrovascular aneurysms, arterial hypertension) (2). To the main links of pathogenesis of these long-term complications belong disorder of the elastic-collagen

framework of the vascular wall: functional disorders of smooth myocytes, changes of the collagen and elastin proportion in the vessel wall with predominance of collagen fibers. As a result of the most fundamental researches, structural features of the structure of the aortic wall were studied very well, both in general and in various segments (3,4). However, until now in the modern scientific literature have still been missing data about the structural state of the vessels of the brachiocephalic trunk in case of aortic coarctation in children of the first year of life.

Purpose of the study: make a comparative assessment of structural changes of the left subclavian artery in normal and in case of hypoplasia of the aortic arch in children of the first year of life.

MATERIAL AND METHODS

In the study were included 35 patients, with hypoplasia of the aortic arch, at the age of 65.4 ± 83.9 days (from 1 to 281 days), average body weight 3.3 ± 1.05 (from 1.85 to 6.4 kg), operated in the central pediatric surgery Meshalkin clinic during 2013-2015 years. All patients underwent surgical correction of congenital heart disease (CHD) - hypoplasia of the aortic arch with a modified reverse flap plasty left subclavian artery under normothermic condititions.

The contraol group consisted of patient at the same age, who died after surgery for other congenital heart defects (n=27).

The fragments of the vessels wall of the brachiocephalic trunk (subclavian artery) obtained intraoperatively in the patient of the main group and at autopsy in patients of the control group, using standart method, fixed in 10% formalin solution in phosphate buffer and embedded in paraffin to obtain blocks. Paraffin sections up to 4 μ m thick were performed on a microtome «Microm HM 550», the sections were stained with standart hemotoxylin-eosin for general light microscopy, and coloring according to Van-Gieson with combined repainting with Orcein. The PAS reaction was performed using the silver impregnation of the sections (according to Gomory) and the Picro-Mallory method. Survary microscopy of the obtained histological preparations on a software microscopic complex: a light microscope

«Imadger M2» ZEISS, digital video camera AxioCamHRc and p/computer «Pentium».

Immunohistochemical stainig was performed on a «Benchmark XT Ventana» automated immunohistotainer using muscle actin (ActinMuscle (HUC-1) and smooth muscle myosin (Myosin, SmoothMuscle (SMMS- 1).

The visualization system «ultraView Universal DAB Detection Kit» (Roche). In stereomorphometric study were assessed features of angioarchitectonics (degree of vascularization), the ratio of elastin and collagen, and changes their ratio in patients of main and control groups.

Statistical analysis

Statistical processing was carried out using the program Statistica 10.0.

Continuous variables were expressed as means $\pm$ standart deviation. In order to determine the statistical significance of differences was used Student's t-test. A value ≤ 0.05 was considered statistically significant.

RESULTS

In histological examination of preparations of the vascular wall of the brachiocephalic trunk was determined statistical non-significant decrease of vascularization degree of the subclavian artery (decreasing a number of the blood vessels in the wall) in patients of the main group (with hypoplasia of the aortic arch), comparing with results of control group (table 1).

Table 1. Structural features of the wall of the left subclavian artery

Indicator	Control (n=27)	Hypolasia of arch (n=35)	P
Vascularization	12.4 $\pm$ 0.35	11.8 $\pm$ 0.41	p>0.05
Collagen fibers	28.3 $\pm$ 6.02	31.7 $\pm$ 5.81	p>0.05
Elastin fibers	52.4 $\pm$ 4.09	42.1 $\pm$ 6.07	p>0.05
The ratio of elastin and collagen fibers	2.1 $\pm$ 0.73	1.3 $\pm$ 0.41	p>0.05

Content of thin collagen fibers (CF) in the wall of normal subclavian artery (control group) was 28.3 ± 6.02 , which is significantly less, than in patients with hypoplasia of arch ($p < 0.05$). In a comparative assessment of content of elastin fibres (EF) in control and main groups was established, that in the wall of pathologically changed artery EF signifivantly more, than in a zone of coarctation ($p < 0.05$). At the same time, in the both group was revealed general trend a decrease of EF content ($p < 0.05$). In the wall of subclavian artery in patients of the main group was revealed hypoelastosis up to the formation of «bald spots» (Figure 1).

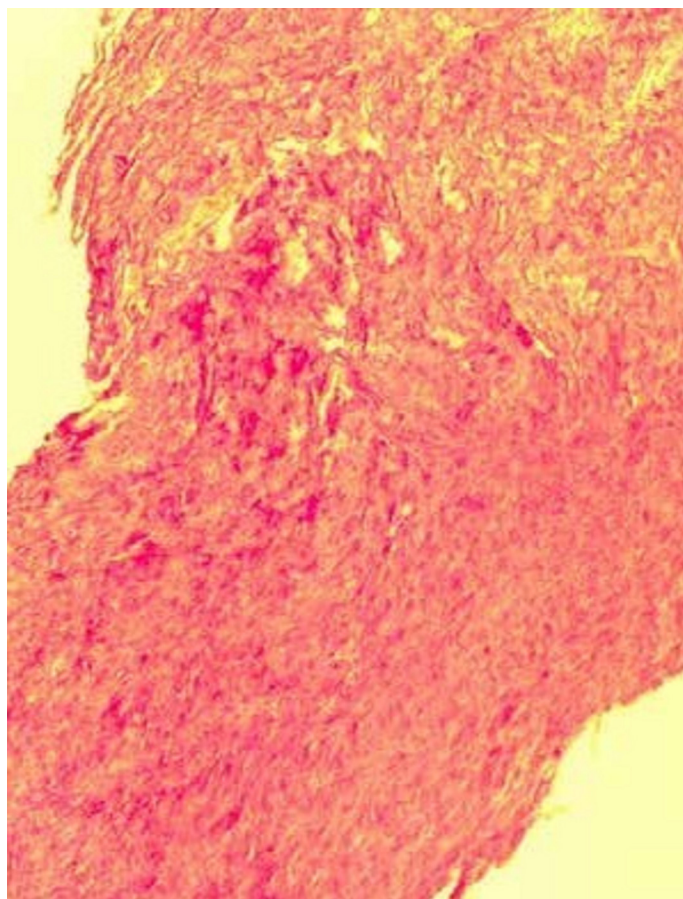


Figure 1. Fragment of the wall of subclavian artery in patients with hypoplasia of aorta arch (hypoelastosis with formation of «bald spots»). Coloring according to Van-Gieson x180

The increasing of content of thin CF in the group of patients with aorta arch hypoplasia indicates a disorder of synthesis of cellular elements of the vessel walls as smooth myocytes (SM) (Figure 2), fibroblasts (FB) and myofibroblasts (MFB). Reason for a disorder of synthesis of cellular elements is a damage of a cellular fibrous structures, proceeding on the background of the disease, which leads to develop the myxomatous muscular fibrous tissue in the inner and middle coat of the subclavian artery (Figure 3), represented by proliferating cellular elements, with the formation of loose connective tissue (CT) around them, containing a large number of thin CF.

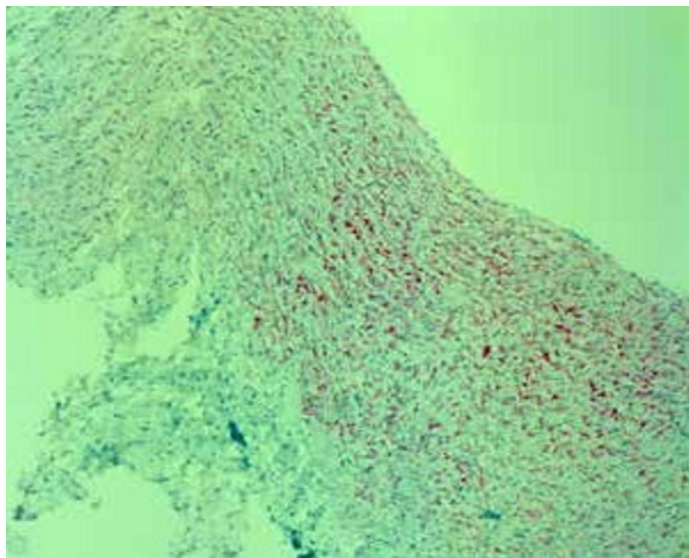


Figure 2. Uneven distribution of myosine in the wall of subclavian artery in patients with aorta arch hypoplasia. Coloring with using Myosin, SmoothMuscle (SMMS-1). Magnification x 180

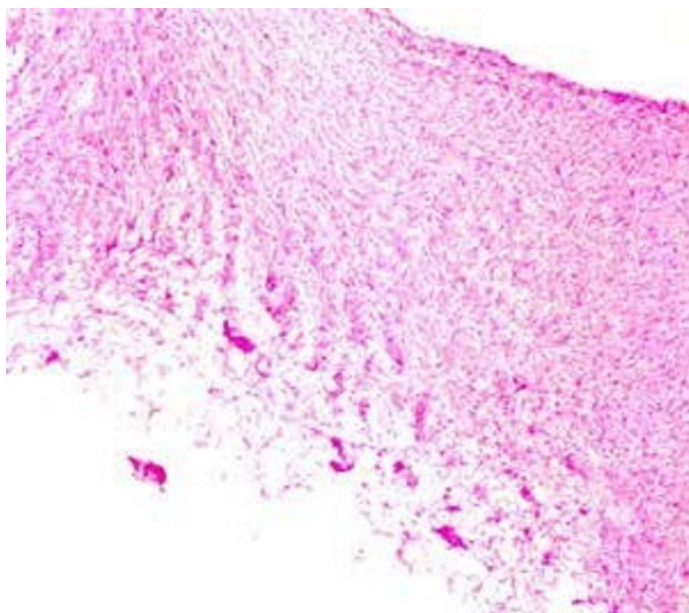


Figure 3. Areas of myxomatous muscular fibrous tissue. Hematoxylin-eosin staining. Magnification x 180.

A feature of angioarchitectonics in the patients of the main group is the fact of neoplasm of capillary-type vessels in the adventitia of the wall of subclavian artery from own vessels with the participation of endotheliocytes (EC), SM and FB of adventitia. This process occurs with a decrease in the number of intramural vessels (Figure 4).

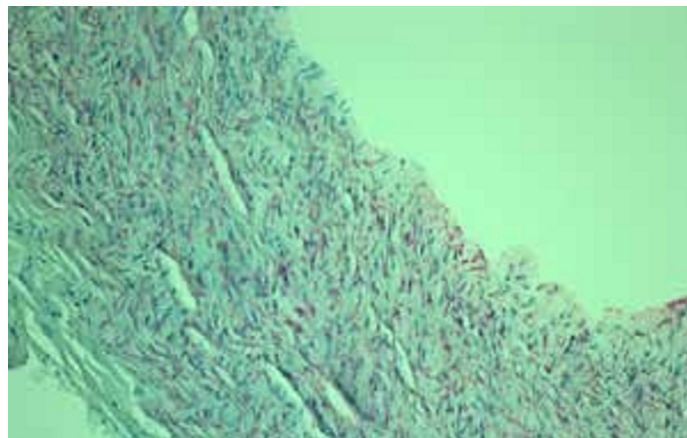


Figure 4. Intramural vessels of the subclavian artery coloring using ActinMuscle (HUC-1). Magnification x 180

As a result of applying Picro-Mallory method was determined that in patients of the main group in the wall of subclavian artery from the side of intima are formed accumulations of lipids and «foamy» cells, which are generally accepted early histological signs of atherosclerosis (Figure 5).

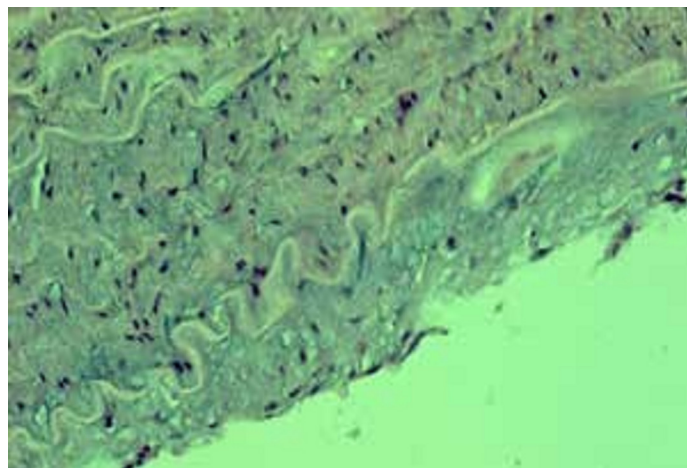


Figure 5. Accumulation of lipids and «foamy» cells in intima of the vessels. Coloring PicroMallorytrichromica. Magnification x 280

The subclavian artery belongs to the vessels of the elastic type, which implies mandatory presence of a collagen-elastin carcass. Its main function is to convey of the pulse wave and smooting «hydrodynamic» impact, i.e. the transformation of the pulsing blood flow into a more uniform. In congenital pathology of the aortic arch occurs a disorder of the collagen-elastin carcass, which leads to the launch of the pathogenesis of vascular dysfunction.

The development of this dysfunction can be single out as a prognostic criterion of long-term prognosis after the correction of aorta arch hypoplasia.

Among of the long-term complications in this type of CHD, more than in 25% of the patients have high risk of early formation of pathology of the cardiovascular system (arterial hypertension, aneurism of the aorta and brachiocephalic vessels, coronary heart disease and ischemic stroke). For the first time, the pathogenesis of vascular dysfunction in CHD was described in detail in study by Gidding S et al. (1985) (5). The researchers were able to identify and describe in detail the pathological vascular reactivity of the forearm and normal reactivity of the vessels of shin in patients of the first year of life with congenital aortic obstruction. Often, in this category of the patients take place morphofunctional, structural disorders of all layers of the wall of large arteries. It is still unclear, what underlies the above complications; pathology of smooth myocytes, fibrous structures, or a combination of them (6). Most of the researchers focuses their attention only on structural changes in the aorta itself, without paying special attention to pathogenetic and structural changes in brachicephalic vessels. However, most likely this problem has the complex character, which is presented in the study (7,8). The obtained of this study results do not contradict the other morphological studies, in which the structural changes in the wall of elastic type arteries of the patients with congenital obstructive pathology of the aortic arch were studied. Data obtained during the study about increasing of collagen fibers and decreasing a number of elastic fibers up to their complete absence, testify that, these changes in the elastin- collagen composition are the main link in the pathogenesis of increased stiffness of the vascular wall and as a result, decreasing in the distensibility of the artery itself.

Even after the surgical correction of obstruction at the level of aortic arch the ratio of the number of elastin and collagen fibers in the vessel wall not increasing, but continues decreasing over time (9). It is known that, physiological feature in young children is decreased number of elastin fibers in the vascular wall; however during growth period is observed a process of increasing the number of these fibers, but this mechanism does not work in children with congenital pathology of the aorta, even if the defect was corrected surgically. These pathogenetically fixed changes in the vascular wall launch the pathogenesis of systemic arterial hypertension (10).

Results of the study by Meyer A.A. led to conclusion that degenerative and proliferative changes in the wall of the brachiocephalic artery and the aorta itself ultimately lead to early disability of patients and mortality in the general population of patients with this pathology.

DISCUSSION

Identified in the course of this study, damages of the cellular-fibrous structures of the vascular wall with developing of the xymatous muscular fibrous tissue in the inner and middle coat

of the subclavian artery represented mainly proliferating cellular elements, which are “effector cells” of chronic inflammation, also vasa vasorum pathology. Similar changes have been described in aortic aneurysms, therefore, it can be assumed that stable activation of proliferation process and changes in the angioarchitectonics of the vascular wall in this category of patients may be a risk factor for the formation aneurysms.

The data, which obtained during histological examination, indicate the presence of early pathomorphological signs of systemic atherosclerosis in patients with congenital aortic obstruction consist with the results of study by Todorov S.S. (2009 y.), who also conducted a morphological analysis of various segments of the aortic wall and identified early signs of atherosclerosis.

CONCLUSION

Thus, structural changes in the wall of subclavian artery in children of the first year of life with congenital aortic arch hypoplasia consist in an increase in the number of collagen fibers against the background of a decrease in the number of elastin fibers. The pathogenesis of these changes is due to the activation of the proliferation cellular structures of the vascular wall (smooth myocytes, myofibroblasts, fibroblasts) and a change in the ratio of their types. Excessive hyperplasia these cellular elements in the inner and middle layers of the vascular wall leads to the formation of muscle-fibrous tissue in them. Changes in angioarchitectonics are most characteristic of the adventitia of the vascular wall, where the total number of intramural vessels decreases and hemorrhages develop. All of the above-listed structural changes in the vascular wall form “vicious circle” and in complex interaction are responsible for reducing elasticity of the vascular wall and for the development of hemodynamic disorders.

Conflict of Interests: The author declares that there are no conflict of interests.

Financial Disclosure: There are no financial supports.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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