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AGE STRUCTURAL FEATURES OF VASCULAR WALL OF THE HUMAN WILLIS' CIRCLE

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RESUMEN

Determinar las particularidades histológicas y morfométricas de la estructura de los vasos del círculo grande del cérebro (polígono de Willis) en el lugar de su bifurcación en personas de diferentes edades. Los vasos del polígono de Willis han sido investigados en 48 muestras de cerebro, sacados de los cadáveres humanos (0-65 años) y divididos en grupos de acuerdo a la edad según la clasificación de la Organización Mundial de la Salud, usando los métodos microscópicos y morfométricos. El factor hemodinámico, que lleva al deterioro del endotelio de los vasos en el lugar de la bifurcación de los vasos del polígono de Willis, sirve de mecanismo inicial en el surgimiento de los engrosamientos de la íntima, que luego se transforman en las placas ateroscleróticas, lo que se nota en las personas de 34 y 35 años de edad.

***Palabras clave**: hombre; cerebro, arterias; polígono de Willis; anatomía.*

ABSTRACT

The aim of this investigation was to determine the histological and morphometric particularities of the brain greater circle (Willis' circle) vessels structure in their bifurcation area in human beings at various age periods. The Willis' circle vessels were studied microscopically and morphometrically in 48 samples of human brains taken from the corpses of subjects aged 0 to 65 years divided into age groups according the World Health Organization classification. The hemodynamic factor leading to the vascular endothelium damage in the bifurcation area of the Willis' circle vessels was determined to be the trigger mechanism for intimal thickenings formation transforming to atherosclerotic plaques in future, being more evident in subjects aged 34-35 years.

***Key words:** human brain; arteries; Willis' circle; anatomy.*

INTRODUCTION

Nowadays the examination of morphologic features of cerebral arteries has theoretical and practical aspects. The cardiovascular diseases mortality rate in relation to the general mortality rate of the population of the Republic of Belarus is about 55% (Mitkovskaya et al, 2008) with prevalence of coronary heart disease and cerebrovascular diseases.

According to the literature in the area of arterial bifurcations of various organs, including the arterial circle of the brain (circle of Willis), intimal thickenings were found with various types of the structure (Petrenko, 2009; Shormanov et al, 2007; Yefimov, 2008). Nowadays there are some opinions about the formation and function of these structures (Campbell et al, 1981; Motavkin and Chertok, 1980; Petrenko, 2009; Shormanov et al, 2007). The results of some scientific investigations mean that thickenings appear at the 5-6 month of prenatal development in places of branching of brain arteries and they are the physiological formations providing the regulation of the brain blood flow (Motavkin and Chertok, 1980).

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Other authors (Petrenko, 2009; Shormanov et al, 2007; Velican and Velican, 1976) consider that intimal thickening is the result of the hemodynamic (mechanical) factor: local turbulences in the area of arterial bifurcations. In some scientific works the thickenings of intima are considered as "normal age changes".

In the literature studied we have not found the description of histological and morphometric features of the arterial wall structure in the area of human cerebral arterial circle bifurcations during various age periods. The present study was carried out for the purpose of the description of the histological and morphometric features.

MATERIALS AND METHODS

Vessels of Willis' circle of 48 autopsies (human brain, age 0-65 years) which have been divided into age groups according to classification of the World Health Organization are investigated by microscopic and morphometric methods.

Histological preparations were studied after staining by haematoxylin-eosine, by Van Gieson's stain and by Unna-Taentzer orcein. Morphometric examination was carried out with analyzer of images «Bioscan» and program Scion Image v.402. The statistical analysis of data was performed with software "Microsoft Excel 2007" and "Statistica 6.0".

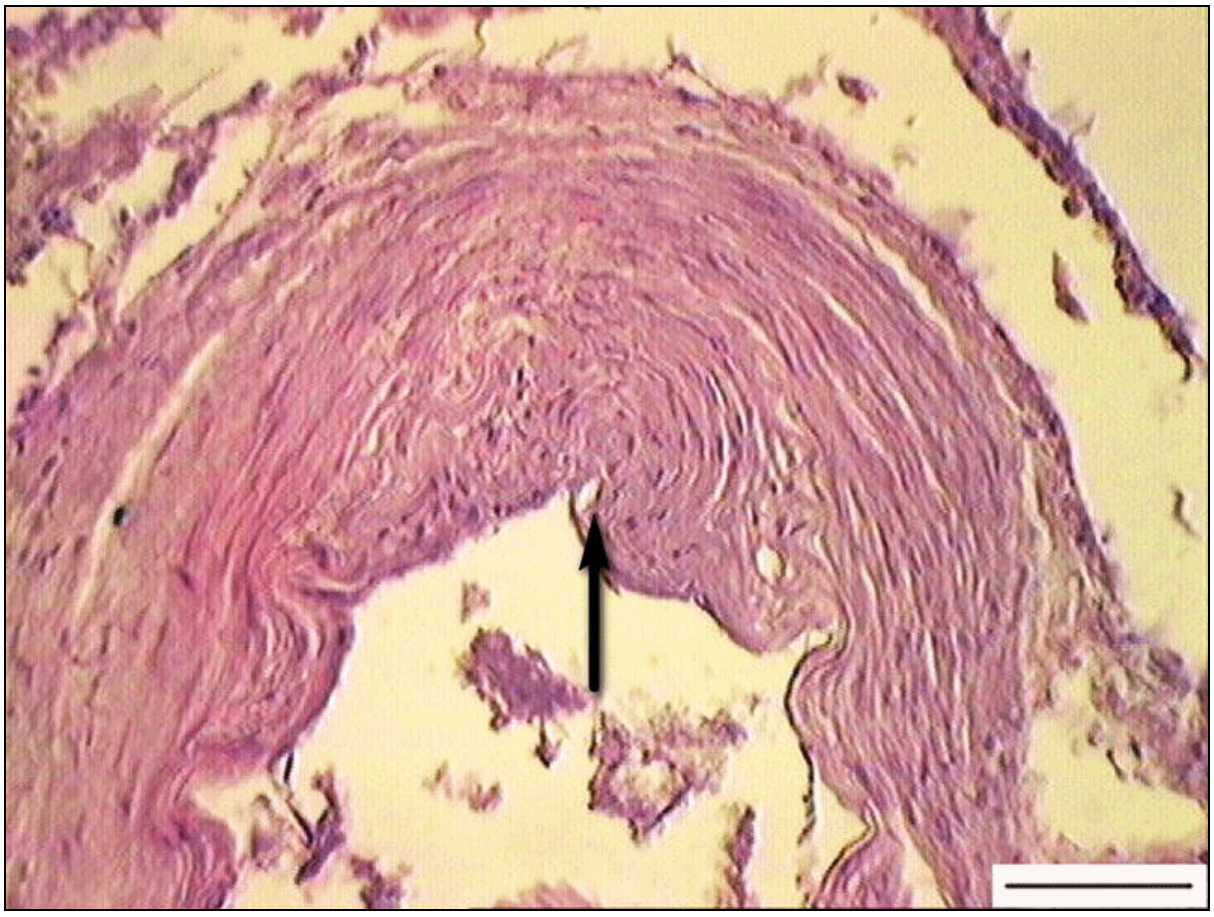
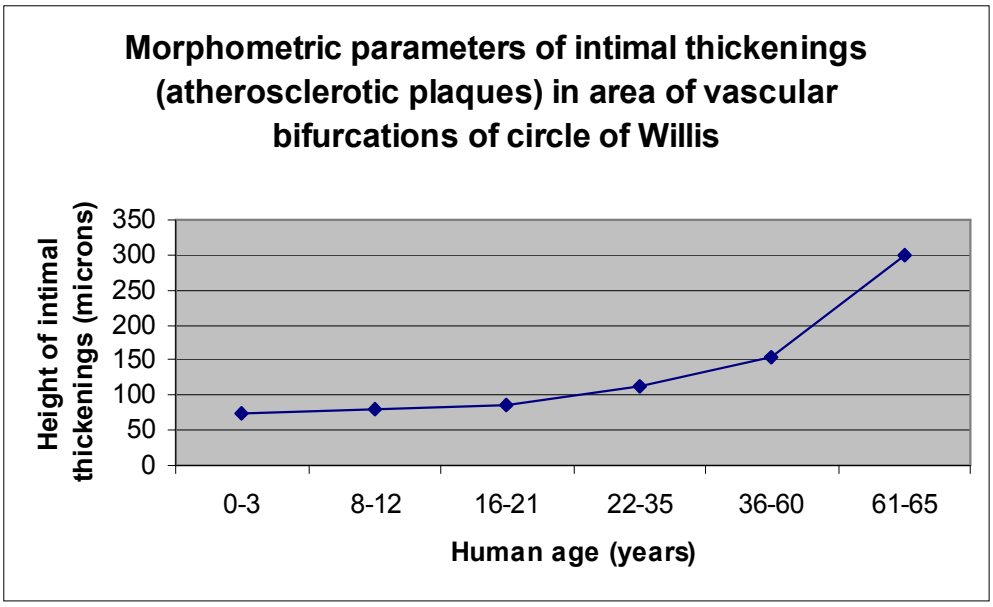


Figure 1 – Intimal thickening in the area of bifurcation of internal carotid artery in a 3 years old infant. Haematoxylin-eosine stain, magnification x 200, ruler 85 microns.

RESULTS

In arterial bifurcation area of Willis circle the thickenings of intima, which are characterized by age features, occurred. At the age of 0 to 3 years in vessels of Willis' circle only 1 to 2 intimal thickenings were found in the area of bifurcation of internal carotid artery (Figure 1).



Graphic 1 – Morphometric parameters of intimal thickenings (atherosclerotic plaques) in the area of vascular bifurcations of Willis' circle.

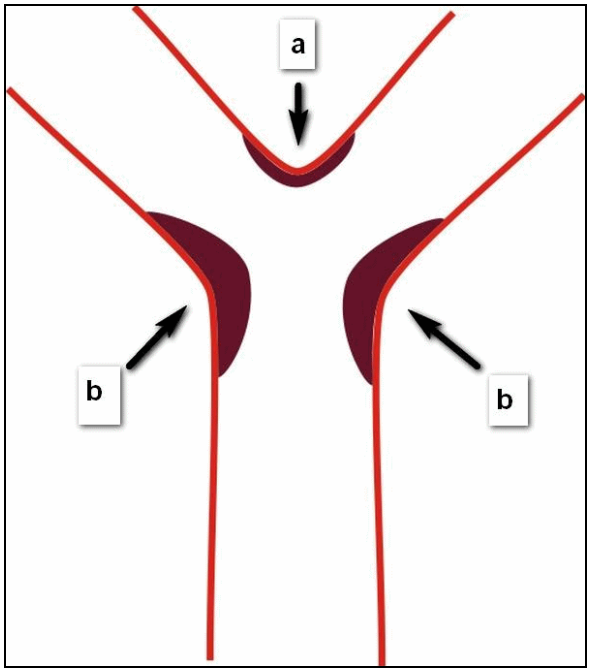


Figure 2 – Localization of intimal thickenings in the area of bifurcation of the basilar artery. **a** – intimal thickenings in the area of apical angle of bifurcation; **b** – intimal thickenings in the area of lateral angles of bifurcation.

In transverse sections of the vessels the height of intimal thickenings varies from 50 to 107 microns (Graphic 1).

Intimal thickenings consist of layers of elastic fibers between which smooth muscle cells are located. Internal surface of thickenings were covered by a layer of endothelium. Internal elastic membrane separated intimal thickenings from the muscular membrane. In infants (0-3 years) this area was 10-20% thinner in comparison with muscular membrane out of arterial bifurcations.

In children of 8-12 years, unlike the previous age period, intimal thickenings were found in the area of arteries bifurcations of Willis' circle both in the area of apical and lateral angles of bifurcations (Figure 2).

The height of intimal thickenings in comparison with the previous period changes were insignificant (80-110 microns). In the longitudinal section of a vessel, the thickenings look like the small hillocks protruding to the lumen of the artery. In the area of apical angle of bifurcations the intimal thickenings were larger than the area of the lateral angles, showing the mechanical influence of the blood stream on the intima of the angle (area of the high shearing stress). In children, the analysis of features of the structure of intimal thickenings of Willis' circle showed changes of interstitial tissue, swelling of elastic fibers, fragmentation of internal elastic membranes and separation of fibres of the intima.

In children, the muscular membrane under intimal thickening is thinner (30-40%) than the thickness

of the muscular membrane of vessels out of their branching.

At the age of 16 to 21 years the intimal thickenings were found also in places of branching of all vessels of the arterial circle of the cerebrum with localization in the area of apical and lateral angles of bifurcations. Their height, in comparison with the previous ages, changed and varied from 80 to 115 microns. The muscular membrane under intimal thickenings was approximately 40-45 % thin in comparison with thickness outside the arterial bifurcations.

At the age of 22-35 years, as it happened at the age of 16-21 years, the intimal thickenings were revealed in all angles of arterial bifurcations of the cerebrum arterial circle; however its height was larger and varied from 90 to 135 microns. At this age period the height of thickenings in the area of lateral and apical angles of bifurcations was approximately identical. The muscular membrane under intimal thickenings continued to become thinner and constituted 50 % of the thickness of the membrane.

At the age of 36-60 years the height of intimal thickenings increased (135-150 microns) and in the area of lateral bifurcations the height of thickenings was larger (140-150 microns) than in the apical angle (135-140 microns) (Figure 3).

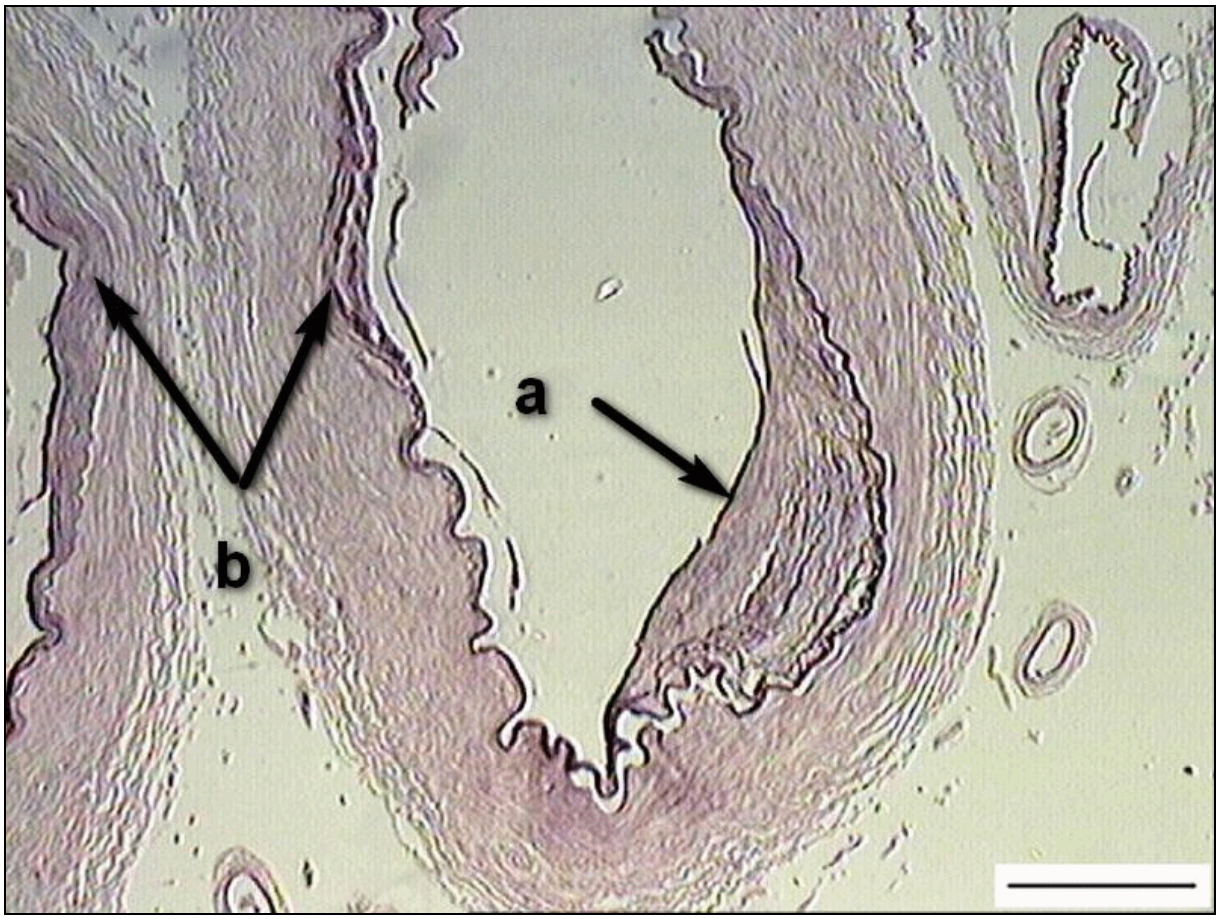


Figure 3 - Localization of intimal thickenings in the area of lateral (a) and apical (b) angles of the bifurcation of the basilar artery. Orcein of Unna-Taentzer method. Magnification x 400, ruler 400 microns.

During this age period the muscular membrane under intimal thickenings became 55-70% thinner than the thickness of the muscular membrane in other structures of the vascular wall.

At the age of 61-65 years the height of intimal thickenings (atherosclerotic plaques) increased in comparison with previous ages, approximately 2–2.5 times, and was 200-500 microns. The muscular membrane under intimal thickenings was considerably thinner (80-90%) in comparison with thickness of the membrane outside the vascular branching of Willis' circle and, some-

times, it was absent. Some intimal thickenings covered the beginning of the arterial branch as a ring or occupied three quarters of the circle of the artery. The atherosclerotic plaques were located in the area of the lateral angles of vascular branching of Willis' circle and protruded to the lumen of the vessel hindering the blood flow. They created the conditions for disturbance of laminar blood flow and influenced the blood stream (pressure) on the wall of an apical angle of bifurcations accelerating the atherogenesis process.

DISCUSSION

Studying the structure of intimal thickenings in the area of arterial bifurcations of Willis' circle, during different age periods, using the hemodynamic laws and literature (Campbell et al, 1981; Ross, 1999; Shormanov et al, 2007; Wellnhofer et al, 2010) we concluded that the hemodynamic factor plays an important role in the genesis of these formations. In the place of natural branching of arteries there is local turbulence of blood flow which lead to endothelial injury or infringement of its permeability, both in the area of apical angle of bifurcations and the area of lateral angles. As a result, in the area of vascular branching, the intimal thickenings were formed by gradually transformation of atherosclerotic plaques. In the area of lateral angles of bifurcations the boundary layer of blood close to intima depends on slow and more chaotic movement, therefore the greatest height of intimal thickenings is observed here.

Some facts proved that the hemodynamic factor plays an important role in occurrence of intimal thickenings. First, at the age of 0-3 years these formations were seldom found in children: 1-2 thickenings in all vessels of Willis' circle. In the next age groups their quantity increased. Thus they were found in the area of bifurcations of all arteries of Willis' circles (both in the area of apical angle and in the area of lateral angles) in the period of 8-12 years old people. Second, the shape and length of the intimal thickenings depend on angle bifurcation type: at obtuse apical angle the length of the thickenings were larger and was caused by a wider area subjected to the action of blood flow on the intima of arteries.

The analysis of research results proved that formation of intimal thickenings begin in children from 0 to 3 years or the last months of prenatal ontogenesis. Later, as a result of growth, the volume of intimal thickenings increased. At the age of 21 years rate of growth of intimal thickenings (thickness) were insignificant and at the age of 22 years there was a considerable jump of growth of these formations. Probably it was connected with neuroendocrinal reorganization and psychoemotional stress during this period and influence of environmental factors (smoking, fat and carbohydrate food abuse, alcohol etc.). The arterial hypertension of any genesis was one of the main reasons of the intimal thickening transformation to atherosclerotic plaques which promote stenosis of vessels that can lead to stroke even at a young age (Hassler, 1962; Ross, 1999; Wellnhofer et al, 2010). In our opinion people having hereditary predisposition to arterial hypertension has early transformation of intimal thickenings to atherosclerotic plaques. But the early transformation was also promoted by oscillatory pressure on the wall of the vessels (compression, stretching, vibration) as a result of changes of pulse pressure that was necessary to be considered according some researchers (Hassler, 1962) as one of the basic factors of atherogenesis.

The normal muscular membrane of a vessel created its skeleton and determined the tonus of a vascular wall. In case of damage the media became the basic target of the cellular reaction including proliferation of smooth muscle cells and migration to media of other types of cells (macrophages, fibroblasts) that leads to its thinning (Ross, 1999; Velican and Velican, 1976; Wellnhofer et al, 2010). The thinning of the muscular membrane of arteries of Willis' circle occured both in the area of lateral and apical angles that also speaks about migration of smooth muscle cells to the intima.

The atrophy of muscular membrane was still probably caused by mechanical influence of blood stream through intimal thickenings in connection with features of blood flow in this area. The process of reduction of thickness of muscular membrane occurred gradually since the birth of humans. However the height of intimal thickenings increased compensating the formed defect of media that was well seen in the area of lateral angles of bifurcations. In the area of bifurcation of apical angle in the place of thinning of muscular membrane under the influence of blood flow an aneurysm could be formed confirming clinical observations (Bazowski et al, 1991; Velican and Velican, 1976).

According to hydrodynamic laws (continuity equation) the blood stream passing through the narrowed site of a vessel and getting to the expanded site reduces speed and leads to the increase of expressiveness of local turbulences. As a result the endothelium of arteries in this place was also damaged leading to the increase in extension of intimal thickenings. It grew from

bifurcations to the part of an artery between bifurcations.

The analysis of research results and literature allow us to make the following conclusions:

1. Intimal thickenings in the area of vascular branching of Willis' circle may be considered as normal age changes.
2. Intimal thickenings appeared in the area of arterial bifurcations of Willis' circle after birth or last months of prenatal ontogenesis under the influence of the hemodynamic factor (local turbulence of blood) which promoted the changes of permeability and damage of endothelium.
3. By the age of 8 to 12 years the intimal thickenings were found in all the branches of the circle in the area of apical and lateral angles. Later the height and area of intimal thickenings increased and the muscular membrane under them gradually became thinner promoting the formation of aneurysms in the area of apical angle of bifurcations under the influence of blood stream.
4. Intimal thickenings were predecessors of atherosclerotic plaques because under the influence of the hemodynamic factor they underwent a degenerative morphological re-organization.
5. The shape and extent of intimal thickenings depended on the angle of arterial bifurcations of Willis' circle (variant of the structure of the circle).
6. Initial displays of atherogenesis in the places of branching of vessels of the arterial circle of the cerebrum were observed at the end of the first and the beginning of the second decades of human life and were accompanied by the separation of fibers, swelling intima and fragmentation of internal elastic membrane. The transformation process of intimal thickenings into atherosclerotic plaques (formation of cavities with atheromatous mass, atherocalcinosis) was found distinctly at the age of 36-60 years.

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