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CLINICAL AND PATHOMORPHOLOGICAL CHARACTERISTICS CARDIOEMBOLIC STROKE

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Abstract. This article presents the most significant risk factors that together contribute to the combined development of ischemic stroke and myocardial infarction: ventricular extrasystole, chronic heart failure, postinfarction cardiosclerosis, atrial fibrillation; the prognostic significance of the thickening of the intima-media complex and the tortuosity of the carotid and vertebral arteries has been proven. The predominance of cardio embolic stroke was established in combination with myocardial infarction, which proceeds with maximum severity, ending in death in more than 3/4 of patients. The high frequency and severity of ischemic stroke in combination with myocardial infarction in women has been proven. The leading risk factors for the combination of ischemic stroke and myocardial infarction are female sex, old age, ventricular extrasystole, chronic heart failure, postinfarction cardiosclerosis, tortuosity of the brachycephalic arteries, thickening of the complex intima-media, duration of hypertension over 7 years in men and 17 years in women, atrial fibrillation.

Ischemic stroke in combination with myocardial infarction often has cardio embolic subtype and clinical picture of severe stroke with disorder of consciousness, the maximum severity of neurological deficiency, serious complications and high mortality. A high frequency of large and extensive supratentorial ischemic lesions in the brain was found in patients with ischemic stroke and myocardial infarction.

Substantiated differentiated approaches to the examination of patients taking into account the risk of ischemic stroke in combination with a heart attack myocardium.

Keywords: ischemic stroke, myocardial infarction, cardio embolic stroke, arterial hypertension, atrial fibrillation.

INTRODUCTION

According to the concept of pathogenetic heterogeneity of IS, heart pathology occupies one of the leading places among the causes of acute cerebrovascular

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accidents (ACV) [4, 3, 9]. With cardiogenic causes of stroke, in its course and prognosis, along with neurological symptoms, extra cerebral complications and conditions play a special role [3]. According to Russian scientists, the frequency of stroke in MI ranges from 1.3 to 12.8%, more often this occurs in the first 2 weeks of the disease [5]. There is evidence that IS itself of a certain localization can cause the development of cardiac complications [13, 16]. From 2 to 6% of patients die of cardiac causes in the first 3 months after acute IS [15]. The complexity of diagnosis in the case of a combination of stroke and MI is associated with the prevalence of more often cerebral symptoms, which greatly complicates the diagnosis of MI. The risk of stroke and MI increases with age. Before the age of 60, stroke was registered in only one third of patients, two thirds of stroke occur at the age of over 60 years [66, 12]. Gender differences in the risk of stroke and MI have been established. The Framingham study showed that the likelihood of developing coronary artery disease in people under 40 years of age is higher in men (48.0%) than in women (31.0%) [3, 11]. The incidence of stroke among men aged 30–69 years is higher [7, 9]. Mortality from cardiovascular pathology in men, and men of working age, is higher than in women. Men are 3–4 times more susceptible to MI than women [3, 8]. However, it is MI that has been considered one of the leading causes of death in women of reproductive age in recent decades [74]. There is evidence that hospital mortality in MI in women is 2.5 times higher than in men [55, 15]. One of the main correctable risk factors for the development of stroke and MI is arterial hypertension (AH) [17, 3, 9, 11, 12]. A direct relationship was found between the risk of vascular accidents and blood pressure (BP): an increase in blood pressure above 115/75 mm Hg. Art. accompanied by a simultaneous increase in the overall risk of vascular and cardiac diseases. The risk of stroke is increased by heart diseases; embolism, which has 30 or more potential cardiac sources, ranks first among cardiogenic factors. In accordance with the classification of J. P. Hanna, A. J. Furlan (1995), they are divided into three main types: damage to the heart valves, heart chambers, paradoxical cardio embolism [3]. The most significant cardiac risk factor is atrial fibrillation. This allowed the authors to identify three possible options for the development of cardiac and cerebral disorders:

1) with MI, circulation disorders occur in the brain (ischemia, hypoxia, edema, necrosis, erythrodiapedetic hemorrhages);

2) with a cerebral stroke, coronary disorders are possible (angina pectoris, changes in the electrocardiogram (ECG), arrhythmias);

3) simultaneous development of MI and cerebral infarction [106]. atrial fibrillation (AF), while the risk of stroke increases by 3–4 times [4, 3, 1,3]. The most common

cause of stroke in MI is cardiogenic embolism. With atrial fibrillation, the contractility of the left atrial appendage decreases, which leads to blood stasis and the formation of blood clots [11]. In the case of cardiogenic embolism, one of the severe subtypes of IS, CEI, develops. CEI is characterized by the rapid development of neurological symptoms (80% of cases) with its maximum severity in the first 5 minutes (47–74%) and ischemic foci of large and medium size, which in 85% of cases are located in the carotid artery basin, more often in the left MCA basin [67,103, 104]. CEI is characterized by a disorder of consciousness at the onset of a stroke and a phenomenon of rapid regression of symptoms, which is called "spectacular shrinking deficit syndrome" and occurs in 12% of patients [40, 153]. A feature of CEI is also hemorrhagic transformation, which is determined in 15% of cases [6,7]. CEI is often accompanied by aphasia, which in turn makes it difficult to contact the patient and collect complaints about MI.

Purpose of the study: to identify risk factors and clinical and morphological features of ischemic stroke in combination with myocardial infarction to justify additions to a differentiated examination of patients in the acute period of the disease.

MATERIALS AND METHODS

The work was performed on the basis of the clinic of the Tashkent Medical Academy. This study is based on the analysis of the results of a comprehensive clinical examination of 105 patients and 138 patients of pathomorphological study. For clinical examination, patients were selected for 5 years. The selection criteria were: 1) patients with ischemic stroke in combination with acute myocardial infarction (main group - MG); 2) persons with ischemic stroke without myocardial infarction (comparison group - CG). Exclusion criteria: oncological and hematological diseases, severe renal and hepatic insufficiency. Of the 105 examined patients, 70 patients were MG with IS and MI, the mean age was 72.2 ± 8.22 years. The CG included 35 people with IS without MI, the mean age was 68.4 ± 5.51 years. Criteria for inclusion in the CG: 1) IS without myocardial infarction; 2) subtypes of IS - in accordance with the diagnostic range of MG; 3) the age of patients older than 60 years - according to the average age of patients with MG.

The surveyed included 55 women and 50 men. In the main group 43 women (61.4%) and 27 men (38.6%) were observed. Average age men - 65.3 ± 7.63 years, women - 76.3 ± 6.17 years. In the comparison group and in the main group, the average age of men and women was comparable: 68.1 ± 6.19 years for men and 69.0 ± 4.33 years for women. In 19 patients with MG (4 men and 15 women), the stroke was recurrent (27.1%). In CG, recurrent stroke occurred in 14 patients (40%): 8 men and 6 women. There was no significant

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difference in the lateralization of the stroke focus in patients with MG: 45.7% had a left hemispheric stroke and 45.7% had a right hemispheric one.
8.6% were diagnosed with ischemic stem stroke. In the comparison group the diagnostic series corresponded to the main group (Table 1).
Localization of ischemic strokes in patients in the main group and the comparison group
Table №1

Group	Number of cases					
	Left hemisphere		Right hemisphere		IS in VBS (stem)	
	abs	%	abs	%	abs	%
MG (n = 70)	32	45,7	32	45,7	6	8,6
CG (n = 35)	16	46,0	16	46,0	3	8,6
P		>0,05		>0,05		>0,05

Patients with MG were more often diagnosed with CEI (70%). In 6 patients with CEI
(8.3%) had hemorrhagic transformation of IS. Less common stroke of unknown etiology (NE) (20%) and LS (10%). ACA in the PMA basin not installed. Atherothrombotic variant of IS was not diagnosed in any patient with MG. The study of the clinical picture of patients with MG included the study of subjective and objective symptoms in comparison with those in HC patients, taking into account gender differences and the priority of stroke or MI. Patients with MG at admission more often (52.9%) complained of weakness in the arm and/or leg, and more often they were men. The second most common was speech disorder (Table 2). 25 (35.7%) patients with MG did not complain due to the severity of the condition, depression of consciousness, aphasia or astrognosia. In the CG, weakness in the arm and leg was also the leading complaint (71.4%), speech impairment also ranked second in frequency (51.4%). In this group, there were only 4 patients (11.4%) who could not complain because of their condition ($p < 0.01$). Only 9 patients of the MG (12.9%) complained of pain in the region of the heart, the rest either did not experience pain or could not report it because of their condition. Patients with HS did not complain of pain in the heart, they often complained of headache (42.9%). In the MG, headache bothered 7 women (16.3%) and 1 man (3.7%), i.e., in general, it occurred much less frequently than in the CG ($p < 0.01$). A more typical complaint for patients with MG was general weakness (22.9%), with approximately the same frequency in men and women (20–25.9%).

HC subjects practically did not complain of general weakness ($p < 0.01$). Asymmetry of the face, which patients called "distortion", bothered 30% of patients in the MG and did not statistically differ from the frequency of this complaint in the CG (28.6%). Patients of both groups complained about the violation of sensitivity, somewhat more often in the SG, without a significant difference ($p < 0.5$), for men and women in the MG this complaint was not typical. (Table 2)

Complaints of patients of the main group and comparison group

Table № 2

	Female (n = 43)		Male (n = 27)		Total (n = 70)		Female (n = 12)		Male (n = 23)		Total (n = 35)	
Complaints												
	abs	%	abs.	%	abs	%	abs	%	abs.	%	abs	%
Headache	7	16,3	1	3,7	8	11,4	5	41,7	10	43,5	15*(1)	42,9
General weakness	9	20,9	7	25,9	16*(6)	22,9	1	8,3	–	–	1	2,9
Chest pain	5	11,6	4	14,8	9*(6)	12,9	–	–	–	–		
Weakness in the arm and leg	20	46,5	17	62,9	37	52,9	6	50,0	19	82,6	25	71,4
Sensory disturbance	5	11,6	4	14,8	9	12,9	2	16,7	5	21,7	7	20,0
"Distortion" of the face	8	18,6	13	48,1	21	30,0	2	16,7	8	34,8	10	28,6
Speech disorders	17	39,5	13	48,1	30	42,9	6	50,0	12	52,2	18	51,4
Dizziness	2	4,6	4	14,8	6	8,6	2	16,7	4	17,3	6	17,1
Impaired coordination	1	2,3	5	18,5	6	8,6	2	16,7	4	17,3	6	17,1
Unsteadiness when walking	1	2,3	3	11,1	4	5,7	3	25,0	6	26,0	9	25,7
Nausea, vomiting	2	4,6	1	3,7	3	4,3	–	–	–	–	–	–
No complaints due to condition	18*(4)	41,8	7	25,9	25*(6)	35,7	1	8,3	3	13,0	4	11,4

Focal symptoms in patients of both groups were predominantly hemispheric and testified to damage to the cortex and subcortical region (Table 3). Central paresis of mimic muscles was the most common in MG patients (90.3%). In second place is anisoreflexia (81.9%), in third place is pathological pyramidal reflexes (70.8%), both were manifestations of central hemiparesis or hemiplegia. Hemiplegia, as the most severe manifestation of damage to the motor sphere, in the MG was statistically significantly more common than mild ($p <$

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0.001) or moderate hemiparesis ($p < 0.01$). In CG, on the contrary, mild hemiparesis prevailed ($p < 0.001$). There were no statistically significant differences between the groups in the frequency of anisoreflexion, but pathological pyramidal signs were more common ($p < 0.01$) in the MG.

In patients with MG, central paresis of the muscles of the tongue was significantly observed, especially in women ($p < 0.05$), and gaze paresis, indicating the vastness of the focus and the severity of the stroke ($p < 0.001$). There was only one patient with gaze paresis in the CG. In both groups, in general, a serious condition was more common in women (75.4%) than in men (46.0%) ($p < 0.01$). 40% of patients with MG were admitted to the hospital with impaired consciousness: stunning occurred in 19 patients (27.1%), stupor - in 8 (11.4%), coma - in 1 (1.43%). At the same time, stupor and coma were observed somewhat more often in women - 7 patients (16.3%) than in men - 2 (7.4%) (not significant, $p < 0.2$). The majority of HS patients did not have impaired consciousness upon admission. Psychomotor agitation occurred in 9 (12.9%) patients with MG: 4 women and 5 men. In second place in frequency after movement disorders in patients of both groups were speech disorders, with aphasia occurring approximately from

the same frequency, and dysarthria predominated in the CG ($p < 0.05$). In both groups, aphasia was more common in women, and dysarthria was more common in men without significant difference (see Table 3). Sensory disorders in the form of hemianesthesia were detected somewhat more frequently (without significant difference) in women in the MG (22.2%). When comparing focal neurological symptoms in the gender aspect, it was found that in women with MG, statistically significantly more often than in men, there was a combination of symptoms: paresis of gaze, language, aphasia, hemiplegia and hemianesthesia, which may indicate a greater severity of stroke and the extent of the lesion. When taking into account the total frequency of severe motor disorders, such as hemiplegia and gaze paresis, a statistically significant predominance of MG was obtained in women (93.8% versus 51.8% in men, $p < 0.001$). Significantly less often in patients with MG, such symptoms of IBS lesions as dysphagia (9.7%), nystagmus (6.9%), anisocoria (5.6%), diplopia (2.7%), hemianopsia (1.4%)), which had no significant differences from those in the CG. Wallenberg-Zakharchenko alternating syndrome was detected in the MG in one patient with IS in the IBS pool (1.4%) (Table 3).

Focal neurological symptoms in patients of the main group and the comparison group.

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Table №3

Symptoms	MG						CG					
	Female(n = 43)		Male (n = 27)		Total (n = 70)		Female(n = 12)		Male (n = 23)		Total (n = 35)	
	1		2		3		4		5		6	
	abs.	%	abs	%	abs	%	abs	%	abs	%	abs	%
Paresis of the gaze	15*(2)	35,7	7	25 9	22***(6)	31,4	0	0	1	4,3	1	2,9
asymmetry NLF	41	95,3	23	85,2	64***(6)	91,4	6	50	14	60,9	20	57,1
Tongue deviation	31*(4)	72,1	15	55,6	46	65,7	4	33,3	12	52,2	16	45,7
Mild hemiparesis	3	6,9	5	18,5	8	11,4	7	58,3	8	34,8	15**(3)	42,9
Moderate hemiparesis	12	26,9	5	18,5	17	24,3	4	33,3	8	34,8	12	34,3
Deep hemiparesis	4	9,3	9*(5)	33,3	13	18,6	1	8,3	4	17,4	5	14,3
hemiplegia	25**(2)	58,1	7	25,9	32***(6)	45,8	0	0	2	8,7	2	5,7
Anisoreflexia	34	79,1	24	88,9	58	82,9	10	83,3	18	78,3	28	80
Pathological pyramid signs	33	76,7	17	62,9	50**(6)	71,4	4	33,3	9	39,1	13	37,1
Hemianesthesia	10*(2)	23,3	3	11,1	13	18,6	1	8,3	4	17,4	5	14,3
dysarthria	13	30,2	12	44,4	25	35,7	6	50	14	60,9	20*(3)	57,1
Aphasia	22	51,2	9	33,3	31	44,3	6	50	8	34,8	14	40

Pathological part. The work was performed in the laboratory of the Republican Center of Pathological Anatomy (Head - Doctor of Medical Sciences, Professor Tursunov Kh. Z). An analysis of 138 sectional cases with GM and myocardial infarctions with AS of cerebral and coronary arteries was carried out. All deceased patients were examined and treated in the intensive care unit, cardioreanimation and intensive neurology department of the TMA clinic for the period from 2014 to 2020. The autopsy of all deceased patients was carried out in the laboratory of the Republican Center of Pathological Anatomy.

The criterion for inclusion in the study was the presence of atherosclerotic plaques in the arteries of the brain and brain infarction. Exclusion criteria from the study were the presence of cerebral hemorrhage, rheumatism, inflammatory diseases and heart defects.

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Among the deceased were 93 men and 45 women aged 38 to 89 years (mean age 63 ± 11 years). The average age of men was 60 years, women - 69 years. The distribution of deceased patients by age group and gender is presented in Table 1.

Table 1. Distribution of deceased patients by age groups and gender

	Age groups, years				
Sex	**38-49**	**50-59**	**60-69**	**70-79**	**81-84**
Male	**16**	**25**	**34**	**18**	**-**
Female	**2**	**7**	**15**	**14**	**7**
Total:	**18**	**32**	**49**	**32**	**7**

In 113 cases (82%), a combination of AS with AH was found at autopsy, in 9 (6.5%) - AS with diabetes mellitus. The cause of death in 64 patients (47%) was a pronounced edema of the GM with displacement and wedging of its trunk and parts of the cerebellum into the foramen magnum, caused by infarction of the GM. The death of 36 patients (26%) was due to massive thromboembolism of the pulmonary trunk and pulmonary arteries from the deep veins of the thigh and leg, 24 (17%) - acute cardiovascular failure associated with myocardial infarction (13 cases) or acute diffuse ischemic changes in cardiomyocytes in combined with small-focal and large-focal cardiosclerosis of the left ventricle (9 cases), 15 - other types of visceral pathology (table 2).

Cause of death of patients	**Number of deaths**
Cerebral edema with dislocation of its trunk	64
Massive thromboembolism of the pulmonary trunk or pulmonary arteries	36
Acute heart failure	22
Acute respiratory failure	6
Acute cardiopulmonary failure	4
Acute renal failure	4
Hemorrhagic shock	**1**
Pericardial hemotamponade	**1**

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The arterial system of the brain in each case was studied at three structural and functional levels: MAG - ICA and PA; extracerebral arteries (arteries of the upper lateral and lower surfaces of the brain, including the arterial (willisian) circle of the brain) and intracerebral arteries; vessels of the microvasculature. Also, the common carotid arteries were studied along their entire length, the aortic arch, the brachial trunk, the subclavian arteries up to the outlet of the PA and CA. In each case, attention was paid to the structure of the circle of Willis, the diameter of the GM arteries, the localization and nature of atherosclerotic changes, the degree of atherostenosis, and the presence of blood clots and emboli (athero or thromboembolism) in the vessel: In addition to the study of the arterial system, an assessment was also made of morphological changes in the heart caused by atherosclerosis of the coronary artery and arterial hypertension.

The degree of atherostenosis was determined visually. According to the degree of arterial stenosis, atherosclerotic plaques were divided into: flat or slightly narrowing artery lumen (atherostenosis <20%); narrowing the lumen of the artery by 20-50%; narrowing the lumen of the artery by 50-70%; narrowing the lumen of the artery by more than 70%. According to the nature of atherosclerotic changes, they were divided into fibrous plaques and complicated atherosclerotic lesions in the presence of hemorrhage into the plaque, ulceration of its cover, decay or calcification in the plaque.

To indicate the localization of atherosclerotic plaques, the ICA is conditionally divided into 4 parts, according to international anatomical terminology [178]: cervical with carotid (carotid) sinus (slightly enlarged section of the artery located at its very beginning); stony, located in the carotid (carotid) canal of the pyramid of the temporal bone; cavernous (cavernous), or carotid siphon located in the cavernous sinus; cerebral (cerebral) part (Fig. 1). The PA is divided into 3 parts: the orifice, extra cranial, and intracranial parts (see Fig. 1).

GM was extracted entirely at autopsy. After fixation in a 10% formalin solution, the brainstem, together with the cerebellum, was separated from the cerebral hemispheres by an incision made at the border between the midbrain and the pons. The GM was cut into 9-10 frontal or 5-6 horizontal blocks through both hemispheres along with the leptomeningx and vessels of the brain surfaces. Incisions through the midbrain, pons, medulla oblongata and cerebellum (4-5 in number) were made perpendicular to the longitudinal axial line, focusing on the anatomical structures visible from the surface (superior and inferior colliculus, inferior olives and pyramids of the medulla oblongata). To detect small-focal changes in the cerebellum, an incision was made through its vermis in the sagittal

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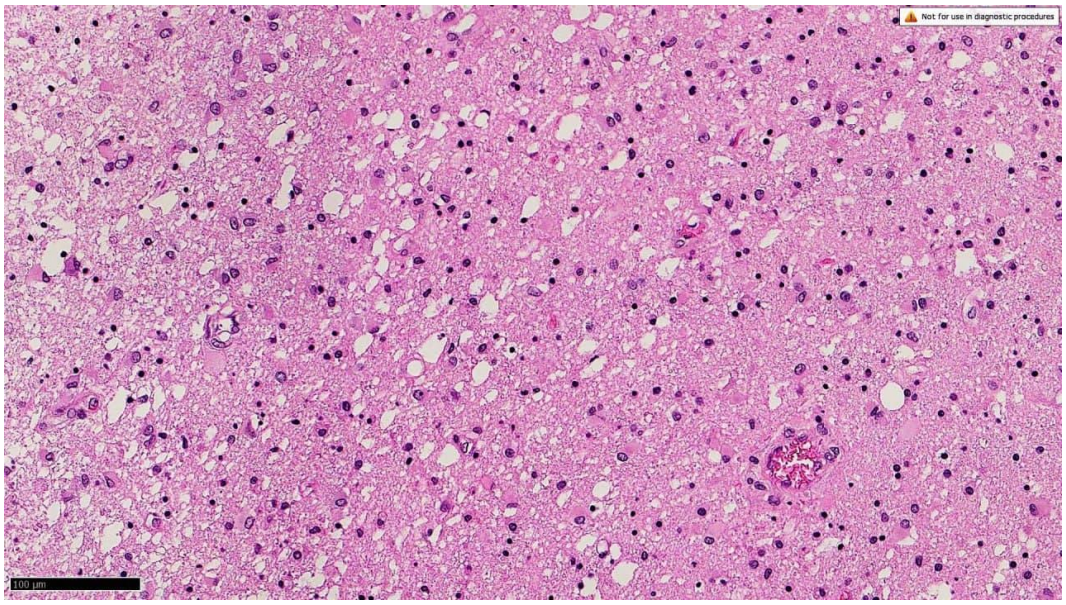
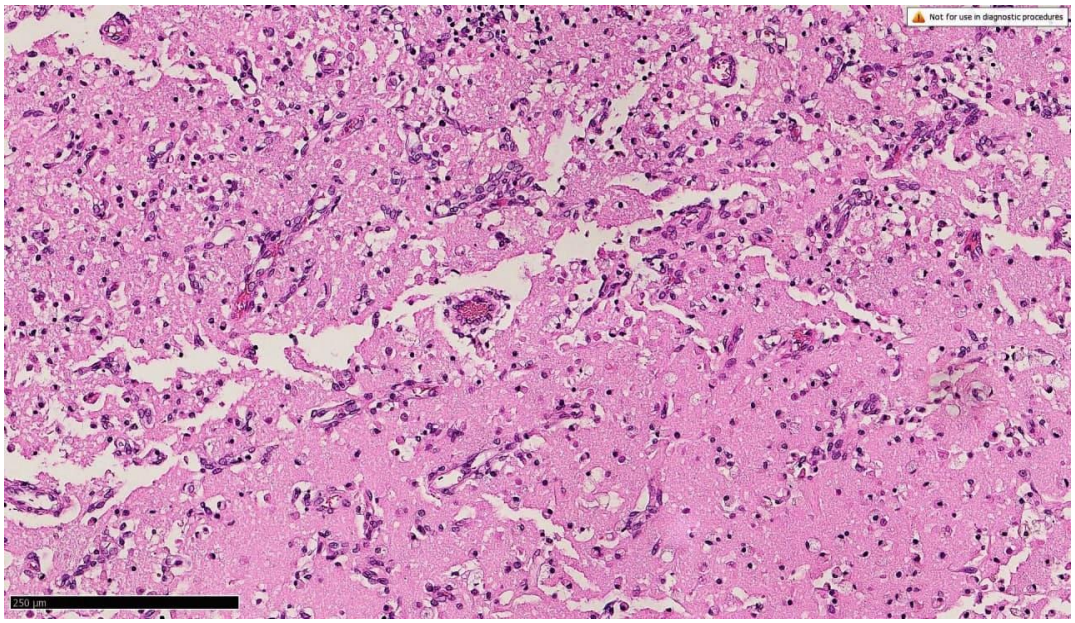
plane and then 2-3 incisions were made through each of its hemispheres at an angle of 30, 45, and 60°C to the sagittal plane.

The results of histological examination.

Examination of the brain in the OG revealed pronounced pericellular and perivascular edema and swelling of the brain tissue, plethora of capillaries (Pic. 1), dystrophy and necrosis of individual cells, and phenomena of satellitosis and neurophagia (Pic 2). In the main lesion - necrosis (Pic. 3).



Pic. 1. Pericellular edema in the form of enlightenment, “spongy” of the intercellular space. Stained with hematoxylin and eosin. Magnification 10x10.



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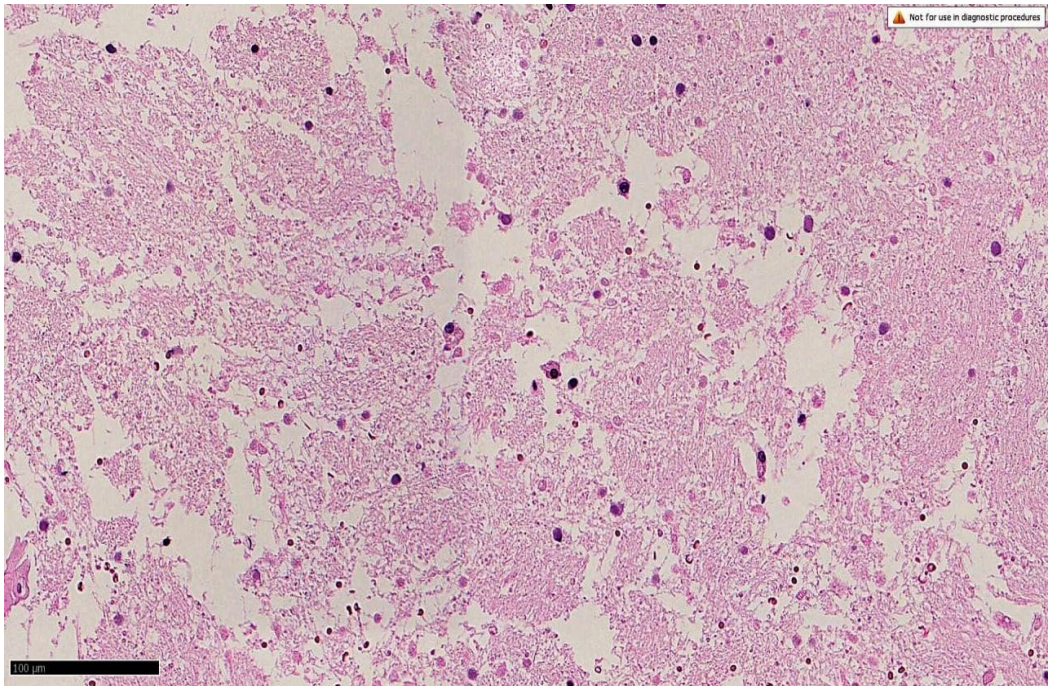
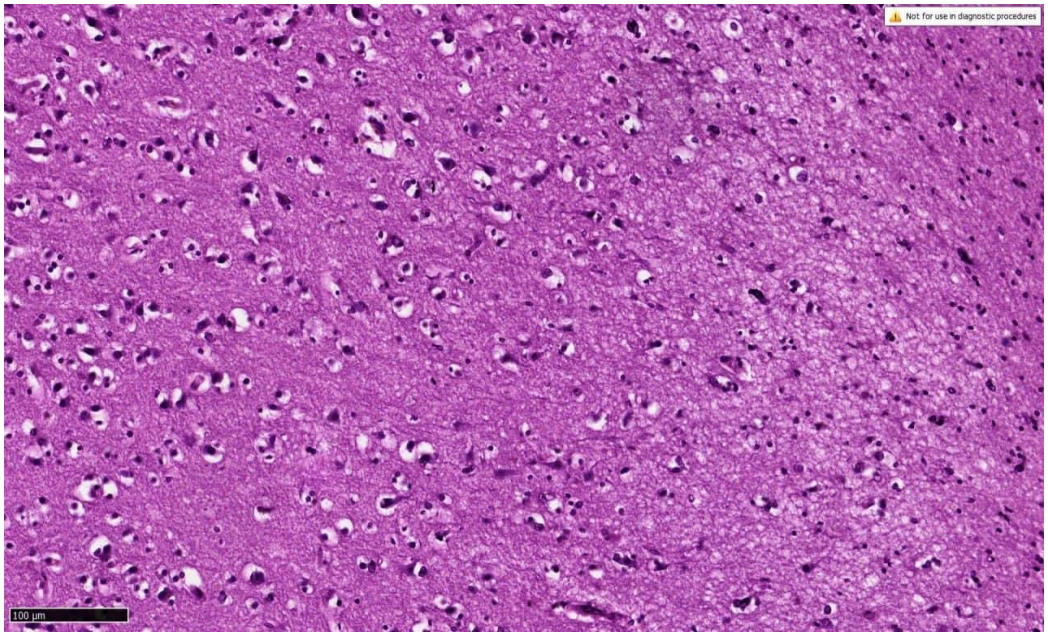
Pic. 2. Pronounced pericellular and perivascular edema. Degeneration and necrosis of individual glial cells, plethora of stasis in the capillaries. Stained with hematoxylin and eosin. Magnification 10x10.



Pic. 3. Necrotized brain tissue with loosening. Stained with hematoxylin and eosin. Increased 10x10.

In the second group (GC), perivascular edema of neurons with focal swelling was detected in the brain tissue (Pic. 4).



Pic. 4. Perivascular edema of neurons and focal swelling of brain tissue, neurophagy phenomena. Stained with hematoxylin and eosin. Magnification 10x10

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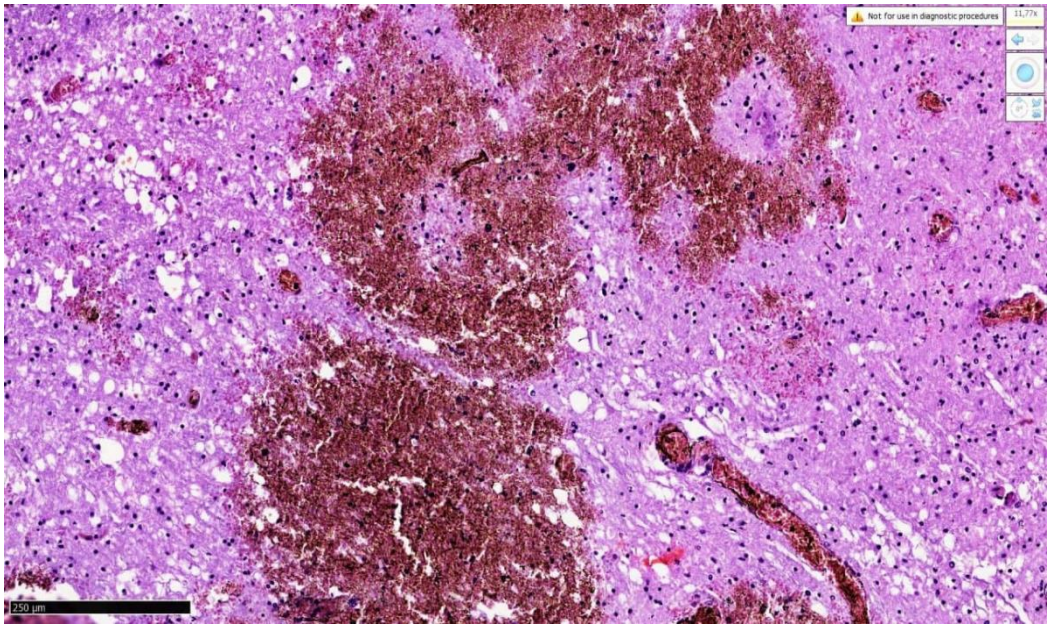
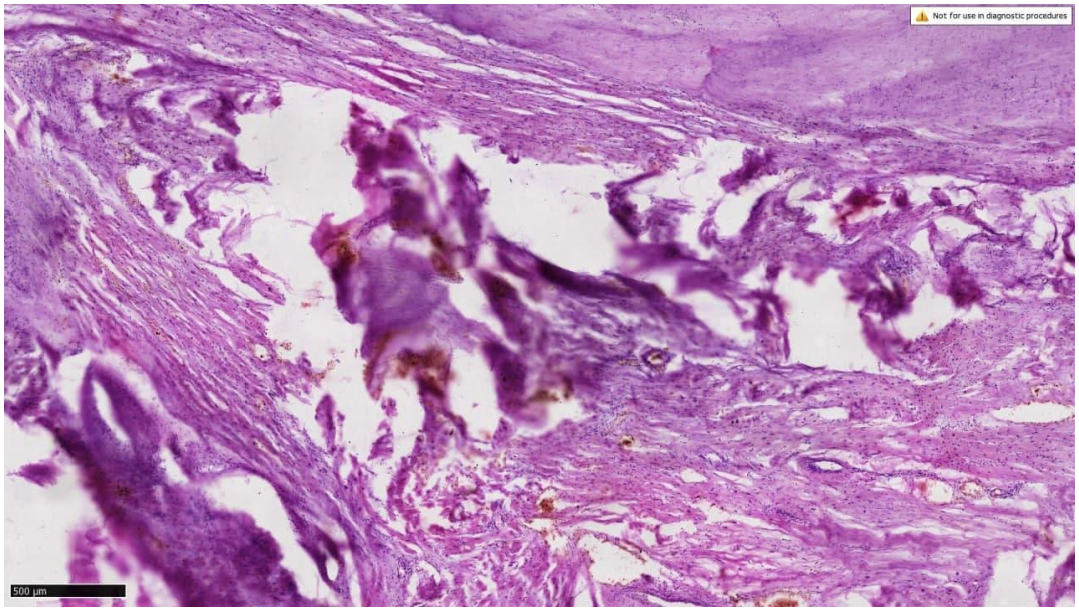
In the capillaries, plethora with stasis and extravasation (Fig. 5).



Pic. 5. Stasis in capillaries with extravasation, perivascular edema of glia. Stained with hematoxylin and eosin. Magnification 10x20.

Histological examination of the heart in patients with OH revealed foci of myocardial necrosis - muscle fibers were swollen, homogeneous, transverse banding was not detected. Cardiomyocytes are non-nuclear, with focal lysis (Pic. 6).



Pic. 6. The focus of necrosis. Stained with hematoxylin and eosin. Magnification 10x10.

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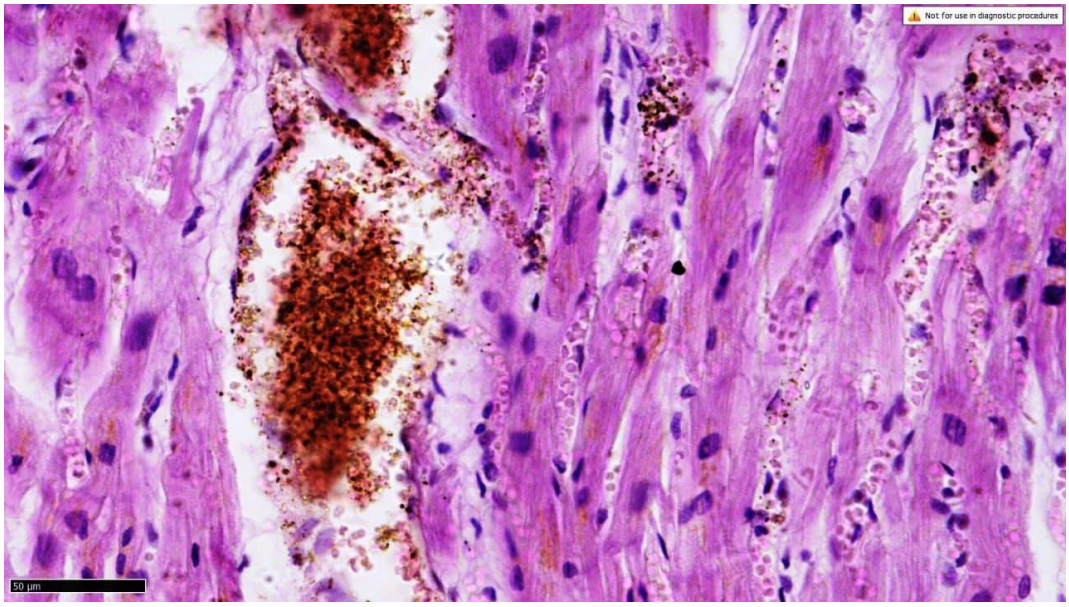
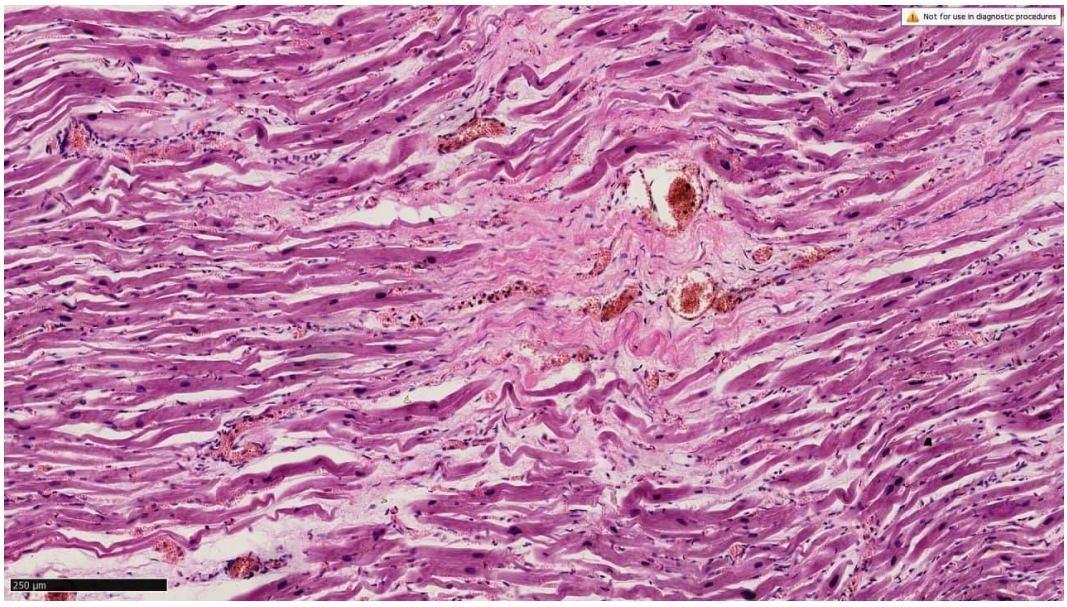
In other areas, hypertrophied muscle fibers and cardiomyocytes with large hyperchromic nuclei, plethora of capillaries with extravasation are found (Pic. 7).



Pic. 7. Hypertrophied muscle fibers and cardiomyocytes, full-blooded capillaries. Stained with hematoxylin and eosin. Magnification 10x20.

In the second group (GC), unevenly hypertrophied cardiomyocytes with small-focal perivascular sclerosis are found (Pic. 8)



Pic. 8. Small focal cardiosclerosis. Stained with hematoxylin and eosin. Magnification 10x10.

In the interstitium of the myocardium, the growth of adipose tissue is noted, mainly around the vessels in which the atherosclerotic process is observed (Pic. 9).

Pic. 9. Focal proliferation of adipose tissue in the interstitium, atherosclerotic plaque in the vessel. Stained with hematoxylin and zosin. Magnification 10x20.

Discussion. Focal symptoms in patients of both groups were predominantly hemispheric and indicated damage to the cortex in the subcortical region; statistically, there were no significant differences between groups in the frequency of anisoreflexia, but pathological pyramidal signs were more common ($p < 0.01$) in the main group.

Cerebral infarctions in atherosclerosis are characterized by a great variety in terms of their localization size, degree of organization, as well as the main factors of their occurrence.

In most cases (67%), infarctions were multiple, in a third of cases single. In 34% of cases, tandem atherostenosis of the arterio-vertebral system was detected, in which stenosing plaques were located in the vertebral artery, basilar artery, cerebellar arteries and posterior cerebral arteries.

One of the severe complications of atherosclerosis is thrombosis. According to the literature, atherothrombotic infarctions accompanied by clinical symptoms account for up to 66% of all ischemic disorders of cerebral circulation.

A comparison was made of the frequency of detection of large-focal cardiosclerosis and myocardial infarction of the left ventricle. With the localization of cerebral infarctions, it was found that large-focal cardiosclerosis is detected somewhat more often when infarctions are localized in the pool only of the artery-vertebrobasilar system (39%). Cardiogenic thromboembolism was detected 2 times more often than arterio-arterial. Thus, based on the results obtained, it can be concluded that the magnitude and localization of cerebral infarction is influenced by the following factors: the number, localization and structure of atherosclerotic

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plaques, the degree of atherostenosis, the localization of a thrombus and embolus, the state of the heart that determines the level of systemic arterial pressure and the possibility of thromboembolism of the cerebral artery, as well as factors such as the state of collateral circulation and structural features of the cerebral arterial circle.

Conclusions. A direct relationship has been established between the localization of cerebral infarcts and the severity of atherostenosis of the cerebral arteries, in the basin of which these infarctions occurred.

The main causes of the occurrence of cerebral infarctions of various sizes were identified: extensive and large infarcts were mainly due to obstructive atherothrombosis, small superficial and deep tandem atherostenosis. The main causes of both single and multiple infarctions in the carotid pool is cardiogenic thromboembolism of the internal carotid artery and its branches, mainly cortical branches of the middle cerebral artery, and obstructive thrombosis, often in the area of ulcerated and hemodynamically insignificant atherosclerotic plaques.

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