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PHYSICAL REHABILITATION OF UPPER LIMB FUNCTION AFTER STROKE, LITERATURE REVIEW

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Abstract: Background. Stroke is an important medical and social problem because its share in the structure of morbidity, mortality and permanent disability is very high [1, 2]. This pathology is traditionally considered to be a disease of elderly patients, since the main risk factors for the development of the disease (atherosclerosis, arterial hypertension, heart rhythm disorders) are more common in people over 45 years of age. However, at present there is an increase in the number of strokes in people of young age (2.5-10% of all cases of stroke).

Key words: Physical rehabilitation of upper limb function after stroke.

Introduction. The main reasons for the interest in the study of stroke in the young are the difference between the etiology of the disease and stroke in older patients; the lack of a clear algorithm for the examination of young patients; and the socioeconomic significance of stroke in persons in the working, reproductive age [3]. The causes of stroke in young and middle-aged patients can be vascular dissections, aneurysms, cardiac pathology, excessive use of some medications (especially oral contraceptives), drug addiction, iatrogenic diseases, tumor embolism, coagulopathies, hereditary diseases, etc.

MELAS syndrome

Etiology and pathogenesis. MELAS (English: mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) is a rare mitochondrial disease that begins in childhood after a normal period of early development and is caused by point mutations in mitochondrial DNA. These mutations result in impaired energy production in the mitochondrial respiratory chain.

Several interacting mechanisms are involved in the pathogenesis: impaired mitochondrial energy production, angiopathy, lactatacidosis, and nitric oxide deficiency [4, 5]. The inability of damaged mitochondria to produce sufficient energy leads to multi-organ pathology. Energy deficiency also stimulates proliferation of smooth muscle and endothelial cells of small blood vessels, which leads to microcirculatory disorders and development of stroke-like episodes [6]. MELAS primarily affects organs and tissues with high energy requirements: the muscular and nervous systems. The pancreas, heart, eyes, liver, and kidneys are also affected.

Symptomatology. Patients are characterized by short stature, muscle weakness, hypotrophy, hypotonia, myoclonias, exercise intolerance, neuropsychiatric retardation, acute or chronic renal failure, cardiac conduction disorders, diabetes mellitus, hypoparathyroidism, sensorineural hearing loss, neuropathies, liver and gastrointestinal tract damage [7].

Stroke-like episodes are the hallmark of MELAS syndrome and occur in 84-99% of patients [8]. They are often accompanied by fever, severe headache, and seizures. Due to the occipital lobe lesion, cortical blindness is a typical symptom. In MELAS syndrome, seizures are common (both during stroke-like episodes and independently of them). Seizures can be focal and generalized, often resistant to therapy [9]. Other symptoms include visual agnosia, prosopagnosia, cortical deafness, auditory agnosia, topographical disorientation, various types of aphasia, and hemispheric neglect. Cognitive

disorders are associated with diffuse brain damage (mitochondrial dementia) and are aggravated by lactatacidosis [10].

Diagnosis. Diagnosis of MELAS is difficult because of the large number of different symptoms, seemingly unrelated at first glance, each of which may debut at different times. Diagnostic criteria include encephalomyopathy, stroke-like episodes, laboratory and histologic evidence of mitochondrial dysfunction, and the presence of mutations in mitochondrial DNA. Collection of family history and MRI are necessary [11]. A sign of mitochondrial dysfunction is an increase in lactate in serum and cerebrospinal fluid of more than 0.45‰ [5, 12].

Skeletal muscle biopsy specimens have "torn red fibers" indicating abnormal mitochondrial crowding and vessels with a strong reaction to succinate dehydrogenase. According to neuroimaging data, the temporal, parietal, and occipital lobes are predominantly affected. Foci of cortical-subcortical localization, not corresponding to the system of blood supply of a certain artery, fluctuating, migrating or disappearing are revealed. Often calcification of basal ganglia is detected.

MRI picture of cortico-subcortical lesions of the right cerebral hemisphere with signs of hemorrhagic impregnation of the cortex in a 15-year-old patient with MELAS. In the cortical plate of the precentral sulcus and in the parieto-occipital region, areas of pathologically increased MR signal, repeating the shape of the gyrus, were visualized. A more pronounced MR signal enhancement is noted on series of postcontrast images.

The diagnosis is confirmed by the results of molecular genetic study of mitochondrial DNA with detection of specific mutations [13].

Treatment. Currently, there is no effective therapy for mitochondrial diseases. Treatment begins with dietary intake, excluding long intervals between meals. Reduce the intake of fats (up to 15-20% of calories) and increase the proportion of carbohydrates (more than 60% of calories). In the acute period use frequent feeding, abundant drinking with additional, including parenteral, administration of glucose. In the acute period of metabolic stroke, various classes of drugs are used: glucocorticoids, drugs to correct acid-base balance, antiaggregants, enzyme inhibitors and so on. There is no clear algorithm for prescribing drugs.

Stroke-like episodes with or without seizures may respond to therapy with nitric oxide precursors (L-arginine, citrulline), which reduce their frequency and severity [4, 14]. Carnitine and coenzyme Q10, widely used in the therapy of MELAS syndrome, have no proven efficacy [6]. Seizures before or during stroke-like episodes should be managed with antiepileptic drugs with low mitochondrial toxicity. If these prove ineffective, other drugs may be added [15].

Antiphospholipid syndrome (APS)

Etiology and pathogenesis. APS is caused by the synthesis of antiphospholipid antibodies to phospholipid determinants of cell membranes or phospholipid-binding proteins of blood (lupus anticoagulant - VA, anticardiolipin antibodies, antibodies to β2-glycoprotein I). It is manifested by recurrent arterial and venous thrombosis and obstetric pathology [16].

Primary and secondary APS are distinguished. The occurrence of primary APS is not associated with comorbidities. Secondary APS occurs in association with autoimmune diseases such as systemic lupus erythematosus and Sjögren's syndrome. It can be caused by certain medications, such as novocainamide, quinidine, hydralazine, isoniazid, aminazine; it occurs in infectious diseases, malignant tumors. Sometimes APS leads to multi-organ failure due to generalized thrombosis. This catastrophic APS (Ascherson syndrome) has a high risk of lethal outcome.

Symptomatology. Thrombosis is the main manifestation of APS. Thrombosis of the deep veins of the lower extremities is the most frequent, especially in the debut of the disease. APS is one of the causes of ischemic stroke (IS) in young people [17]. Antiphospholipid antibodies (aFL) are detected in 18% of AI cases in young patients [18]. In aFL-positive patients, MRI may show cerebral infarcts similar to the pattern of multiple sclerosis. In addition, APS can cause AI in the neonatal period [1,9]. APS can

also occur in elderly patients, which should be taken into account when prescribing angioplasty and stenting, which should be avoided in this syndrome [2]. The combination of APS with MI is an unfavorable prognostic sign.

Neurologic manifestations of APS include cerebral vascular thrombosis leading to I.I. Although the 2006 update of the classification of criteria for APS and its neurologic manifestations includes only transient ischemic attack (TIA) and AI. classification of criteria for APS and its neurologic manifestations lists only transient ischemic attack (TIA) and I.I., a wide variety of neurologic disorders occur in patients with APS: Headache, migraine, bipolar disorder, transverse myelitis, dementia, chorea, hyperkinesias, epilepsy, multiple sclerosis, psychiatric and cognitive disorders, Tourette syndrome, Parkinson's disease, muscular dystonia, transient global amnesia, obsessive-compulsive disorder, and leukoencephalopathy [12]. Multiple lesions are associated not only with vascular thrombosis but also with immune-mediated changes in basal ganglia function, resulting in motor, behavioral, and cognitive disorders [13].

Diagnosis. The diagnosis of APS in a patient requires the presence of thrombosis or pregnancy complication and one serologic criterion (antibodies to cardiolipin - aCL, to β2-glycoprotein I, VA) detected in two blood tests taken 12 weeks apart [4]. Phosphatidylserine-dependent antiprothrombin antibodies can also be used to confirm APS [5].

The aFL profile determines the level of risk for thrombosis. At high risk, there is VA positivity, positivity of three types of aFL, isolated persistent positivity for aCL in high and intermediate levels. At low risk, there is isolated periodic elevation of each of the aFL in medium and low levels [6].

Brain CT scan of a patient with primary APS, renal thrombotic microangiopathy, and primary fetal loss syndrome. The patient had multiple AIs with left-sided hemiparesis and vestibulo-atactic syndrome. The tomogram showed areas of reduced density in the projection of the cortex and the underlying white matter of the right frontoparietal region, foci of weakly reduced density in the white matter of the brain of both parietal and frontal regions.

Treatment tactics. The optimal antithrombotic tactics and intensity of anticoagulation in the treatment of APS-related AI remain uncertain. The risk of bleeding with increasing intensity of anticoagulant therapy must be balanced against the risk of profound disability and death or irreversible neurologic deterioration from recurrent stroke. Current guidelines recommend achieving a target international normalized ratio (INR) level of 2.5 [7].

According to the recommendations issued in 2011. American Heart Association and American Stroke Association, patients with cryptogenic MI or TIA who have a positive aFL test should receive antiplatelet therapy. At the same time, oral anticoagulants are administered to patients with MI who meet all criteria for APS, with the target INR level of 2.0-3.0 being achieved [8].

Treatment of patients with thrombosis and AFL with serologic markers at low levels does not differ from the therapy of AFL-negative patients with similar thrombosis [9]. Patients with established APS and first venous thrombosis are prescribed vitamin K antagonists until an INR between 2.0-3.0 is achieved. An INR level >3.0 offers no advantage over an INR of 2.0-3.0 for the prevention of recurrent thrombosis, but increases the risk of hemorrhagic complications [10].

During pregnancy, low-molecular-weight heparin and low-dose aspirin are used instead of warfarin, which penetrates through the placenta and has teratogenic effect. In the postpartum period in APS for secondary prevention of thrombosis for life vitamin K antagonists with a target INR 2.0-3.0 for venous thrombosis and INR >3.0 for arterial thrombosis are prescribed. When prescribing warfarin with aspirin, the risk of bleeding should be assessed in advance. Rituximab may be effective in resistant forms in the postpartum period.

Catastrophic APS (CAFS) is fatal in 30-50% of cases [11], therefore early diagnosis of CAFS and aggressive therapy are important. The following three goals are pursued: elimination of precipitating factors (use of antibiotics when infection is suspected, amputation of necrotic tissue, suggestion of

APS in patients undergoing surgery or an invasive procedure); prevention and treatment of thrombosis; and suppression of the cytokine "storm" [12].

Currently, in the treatment of CAFS it is customary to first use intravenous heparin, replacing it then with oral anticoagulants, corticosteroids, plasmapheresis, intravenous gammaglobulin, in the presence of lupus erythematosus cyclophosphamide is used [13]. In resistant forms, rituximab, eculizumab are taken. In the absence of infection, antibiotics are not prescribed. In case of ineffectiveness of long-term warfarin (INR >3.0), low-molecular-weight heparins may be prescribed. Promising is the use of direct inhibitors of thrombin and factor Xa. Additionally, hydroxychloroquine, statins [9], peptides blocking pathogenic aPL subpopulations [4] are prescribed.

Although direct oral anticoagulants are an attractive alternative to vitamin K antagonists, their use requires caution . Direct thrombin inhibitors are promising, but they are not yet approved for patients in terminal renal failure . The combination of anti-Xa inhibitor and corticosteroids may be an alternative treatment for cerebral sinus thrombosis and arterial thrombosis in warfarin-resistant APS [7].

Recombinant tissue plasminogen activator (alteplase) is the only approved drug for the treatment of acute AI, but it is rarely prescribed not only because of the small therapeutic window but also because of multiple contraindications, particularly thrombocytopenia. However, in some cases, this drug can be used in patients with APS [8].

Prevention of thrombosis in APS is aimed at eliminating risk factors (hyperlipidemia, arterial hypertension, sedentary lifestyle, smoking, taking oral contraceptives). Primary prophylaxis in aFL-positive patients should be individualized, taking into account specific risks. Hydroxychloroquine, vitamin D, and statins can be used as adjuvant therapy [9]. All carriers of aFL should carry out thrombosis prophylaxis before prolonged immobilization, surgical interventions, in the postpartum period, eliminate cardiovascular risk factors [10]. In asymptomatic aFL-positive pregnant women, hydroxychloroquine is prescribed for primary thromboprophylaxis [11], and prophylactic doses of heparin are administered if the risk of thrombosis is high [12]. Dabigatran, rivaroxaban and apixaban can be used for the prevention of AI.

CADASIL syndrome

Etiology and pathogenesis. CADASIL (English: cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is an inherited autosomal dominant syndrome characterized by cerebral arteriopathy, subcortical infarcts and leukoencephalopathy.

The disease is caused by mutation of the Notch3 gene on chromosome 19, which leads to changes in the structure and function of the transmembrane protein. Calcium channel function is impaired, resulting in arteriopathy and leukoencephalopathy. Degeneration of smooth muscle fibers of vessels occurs. There is occlusion of small perforating vessels of the cerebral white matter, leading to chronic hypoperfusion; the blood-brain barrier is broken [13]. Sometimes large cerebral arteries can also be affected [14].

Symptomatology. Depending on the stage of the disease, the following clinical manifestations are noted. At stage I, at the age of 20-40 years, patients have migraine headache, MRI of the brain may reveal hypointense foci in the white matter near the basal ganglia, periventricularly, in the pontine.

At stage II, at the age of 40-60 years, AI, mental disorders develop; the lesion of the white matter of the brain and basal ganglia increases. After the development of AI, the frequency and severity of migraine attacks usually decrease. I.I. is characterized by the absence of cardiovascular risk factors, recurrent course, lacunar nature, clinical remission in a few days. Hemorrhagic stroke develops very rarely.

In stage III, at the age of 60-80 years, dementia (memory, speech, attention, behavioral disorders) [6], depression, anxiety, gait disorders, urinary incontinence, spasticity, pseudobulbar palsy join.

CADASIL can be suspected if at least two of the following clinical symptoms are present: recurrent MI, migraine, mood disorders, subcortical dementia, large hemispheric white matter lesions, and absence of cortical infarcts on MRI [7]. The syndrome is considered to be reliably established in the presence of the above signs, a detected genetic mutation and/or arteriopathy with characteristic granular osmiophilic inclusions on skin or muscle biopsy [8].

Diagnosis. Leukoaraiosis is a characteristic neuroimaging sign of CADASIL syndrome, but sometimes there may be no changes on MRI tomogram [9]. Electron microscopy of skin biopsy specimens reveals characteristic granular osmiophilic inclusions among degenerated smooth muscle cells of the dermal arteriolar wall [10]. These factors are absent in arterial hypertension and Binswanger's disease.

Due to the high specificity but low sensitivity of electron microscopy, it is necessary to perform repeated studies of biopsy specimens from different areas of the body. DNA diagnosis is the most informative. Predictors of new AI are active smoking, the number of affected brain areas; predictors of disability - gait disturbance, dementia.

Treatment. There is no specific therapy. Antiaggregant therapy (aspirin) is prescribed, which slows the course of the disease and prevents the development of AI, but it increases the risk of intracranial hemorrhage. Pentoxifylline is used to improve microcirculation. Angiography, taking anticoagulants can provoke cerebrovascular disorders. Intravenous thrombolytic therapy is contraindicated because of the possible development of hemorrhagic stroke, although there are reports of its success [12].

Treatment of migraine in CADASIL syndrome is carried out according to generally accepted schemes. In cases of emotional disorders, sedatives, antidepressants are used.Due to the fact that patients have an increase in the level of homocysteine in the blood, it is necessary to treat with folic acid. L-arginine can be used to relieve headache [54].

Conclusion

Genetic causes of stroke in persons of young age are a complex problem requiring joint solution by physicians of different specialties. Increasing the efficiency and availability of enzyme- and DNA-based diagnostics will help to identify many atypical and monosymptomatic cases encountered by practicing physicians. Symptomatic or pathogenetic therapies have now been developed for many inherited diseases, making their timely diagnosis fundamentally important for improving a patient's future prognosis.

Obviously, significant progress will be achieved as metabolic and metabolic, enzyme replacement therapy is improved, and in the future - gene therapy and medical and genetic counseling.

Literature:

1. Ilkhomovna, K. M., Eriyigitovich, I. S., & Kadyrovich, K. N. (2020). Morphological Features of microvascular Tissue of the Brain at hemorrhagic stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 2(10), 53-59.
2. Kadyrovich, K. N., Erkinovich, S. K., & Ilhomovna, K. M. (2021). Microscopic Examination Of Postcapillary Cerebral Venues In Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 3(08), 69-73.
3. Камалова, М. И., & Хайдаров, Н. К. (2020). Prevention and risk factors for brain infarction (literature review). Журнал неврологии и нейрохирургических исследований, 1(2).
4. Ismoilov, O. I., Murodkosimov, S. M., Kamalova, M. I., Turaev, A. Y., & Mahmudova, S. K. (2021). The Spread Of SARS-Cov-2 Coronavirus In Uzbekistan And Current Response Measures. The American Journal of Medical Sciences and Pharmaceutical Research, 3(03), 45-50.
5. Shomurodov, K., Khaidarov, N., & Kamalova, M. (2021). The formation and eruption of baby teeth in children. Збгрник наукових праць SCIENTIA.

6. Khodjieva D. T., Khaydarova D. K., Khaydarov N. K. Complex evaluation of clinical and instrumental data for justification of optive treatment activites in patients with resistant forms of epilepsy //American Journal of Research. USA. – 2018. – №. 11-12. – С. 186-193.
7. Kamalova M. I., Khaidarov N. K., Islamov S. E. Pathomorphological Features of hemorrhagic brain strokes //Journal of Biomedicine and Practice. – 2020. – С. 101-105.
8. Kasimov, Arslanbek; Abdullaeva, Nargiza; Djurabekova, Aziza; Shomurodova, Dilnoza//Features of diagnosis and clinic of post-traumatic epilepsy against the background of concomitant somatic diseases. International Journal of Pharmaceutical Research (09752366) . Jul-Sep2020, Vol. 12 Issue 3, p1788-1792. 5p.
9. Kasimov Arslanbek Atabaevich, Bozorova Sabohat Normo'min qizi, & Gulkhayo Eshmatovna Zhumanova. (2022). Results of a study of clinical and neurophysiological changes in patients with post-traumatic epilepsy with concomitant somatic diseases on the basis of complex drug therapy. World bulletin of public health 10, 186-190
10. Kasimov Arslanbek Atabaevich. (2022). Dynamics of clinical and neurophysiological changes against the background of complex medical therapy in patients with posttraumatic epilepsy with concomitant somatic diseases. Frontline Medical Sciences and Pharmaceutical Journal, 2(03), 78–87.
11. Khudaynazarova Muattar Tokhirjonovna, Ruziyev Jononbek Elmurodovich, & Kasimov Arslanbek Atabayevich. (2022). Peculiarities of diagnosis and clinical picture of posttraumatic epilepsy against the background of concomitant somatic diseases. World bulletin of public health, 10, 121-126.
12. Uralov, F. S. ., Khurramov, M. B. ., Kasimov, A. A. ., & Mamurova, M. M. . (2022). Modern Methods of Epilepsy Treatment and Prevention of Tactical and Therapeutic Errors in Epilepsy Treatment. International Journal Of Health Systems And Medical Sciences, 1(4), 374–377.
13. Шомуродова Д. С., Джурабекова А. Т., Мамурова М. М. Особенности и прогноз поражения нервной системы у беременных женщин с преэклампсией характеризуемые методами функциональной диагностики //журнал неврологии и нейрохирургических исследований. – 2020. – Т. 1. – №. 2.
14. Мамурова, М., Рузиева, Ш., Олланова, Ш., Хакимова, С., & Джурабекова, А. (2015). Клинико-неврологические особенности Хронических цереброваскулярных заболеваний, обусловленных Артериальной гипертензией, у пациентов молодого возраста. Журнал вестник врача, 1(4), 39–42.
15. Мамурова М. М., Джурабекова А. Т., Игамова С. С. Оценка когнитивных вызванных потенциалов головного мозга (р-300) у лиц молодого возраста с артериальной гипотензией //журнал неврологии и нейрохирургических исследований. – 2021. – Т. 2. – №. 1.