SYSTEMIC THROMBOLYTIC THERAPY OF ISCHEMIC STROKE. CASE REPORT (REGIONAL VASCULAR CENTER, YAKUTSK)

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Abstract. Systemic thrombolytic therapy can significantly reduce the degree of neurological deficit and improve outcome in patients with ischemic stroke. The effectiveness of this method was illustrated by the presented clinical report of systemic thrombolysis held in ischemic stroke patient in Regional Vascular Centre, Yakutsk. The "dramatic" decrease of focal symptoms (NIHSS score 2 points) occurred after thrombolysis in 44-old-year patient had initial severe neurological deficits (hemiplegia, hypoesthesia, dysarthria, gaze paresis (NIHSS score 15 points)). This led to the full recovery of lost function and to the independence of the patient's daily life. Thus, systemic thrombolytic therapy can significantly reduce the degree of neurological deficit and improve outcome in patients with ischemic stroke. In Yakutia the number of performed procedures and the result of reperfusion therapy in ischemic stroke will depend from the timely and coordinated work of many pre-hospital and hospital specialists, and from the degree of public awareness about the first signs of a stroke. Another important objective is the introduction of new reperfusion methods in ischemic stroke, including intra-arterial thrombolysis, mechanical clot extraction and combined thrombolytic therapy, in Regional Vascular Center.

Key words: ischemic stroke, thrombolytic therapy, systemic thrombolysis.

Introduction. Pathophysiological basis of ischemic stroke is a cerebral vessel occlusion due to thrombus or embolism, which leads to a decrease of blood circulation in the relevant section of the brain and to the subsequent development of ischemic stroke. The use of methods of reperfusion in the first hours of the disease promotes the prevention or minimization of the extent and severity of brain damage [4]. Currently, the most effective method of restoring blood flow in the occluded

cerebral vessel is reperfusion with thrombolytic agent rt-PA (recombinant tissue-type plasminogen activator) [2].Since recently, systemic thrombolytic therapy (TLT) is used in the first 4.5 hours of the onset of symptoms. Increasing the time of "therapeutic window" (from 3 hours to 4.5 hours) for systemic thrombolytic therapy was made on the basis of recent studies ECASS III, which was completed in 2008 [5]. Selective thrombolysis techniques contribute to the clot lysis in a wider «therapeutic window» and to the possibility of individual dosing of fibrinolytic drug that will promote to reduces the risk of symptomatic hemorrhagic complications [1].

Case Report. We present the results of the systemic thrombolysis therapy case in acute ischemic stroke held at the Regional Vascular Center (RVC), Yakutsk.

Patient T., 44-year-old, citizen of Yakutsk, Russian nationality, a security guard, admitted to RVS on November 4, 2012 at 14:42.The patient had complaints to the weakness in the left limbs and headache at the admission to hospital.

History of present illness: Onset of clinical symptoms occurred at 13:52 in November 4, 2012. The weakness in the left-sided limbs, "twisted" face appeared suddenly. Ambulance was called immediately. It arrived to the patient at 14:03.Doctor had diagnosed the acute stroke, and then patient was transported to a hospital during 39 minutes. The team consisting of a neurologist on duty, intensive care doctor and nurse began examination of the patient at 14:42 in the RVS's admission room.

The patient's condition on admission regarded as bad. Physical examination. General: The skin and visible mucosa: normal color, moderate humidity, clean. No cyanosis or peripheral edema noted. Body temperature was 36.1 C є. Breathing was independent, effective. Lungs: clear to auscultation. Respirations were 18.Heart: regular rate and rhythm. Blood pressure (BP) on the right (D): 160/80 mm Hg, blood pressure on the left (S): 150/80 mm Hg. Pulse was 100.Saturation ($Sp0_2$) – 97%. Abdomen: soft and non tender. No hepatomegaly noted. Good bowel sounds present. Sign Pasternatsky negative on both sides. Urination: free and painless. Overweight: height – 170 cm, weight - 85 kg, body mass index (BMI) - 29.4.

Neurological status: The patient was alert. He was oriented to time, place and person. Cranial nerves: Eye gap equal. Pupils uniform, photoreaction alive. Eyeballs rejected to right, gaze paresis to left. No nystagmus noted. Left corner of the mouth was omitted. The tongue was rough to the left strongly. Speech disorders: dysarthria. Positive symptoms of oral automatism noted. No active left extremity's movement noted: left-sided hemiplegia. Muscle tone was reduced in the left extremities. Tendon reflexes were reduced in the left extremities. Sensation: left extremity's hypoesthesia. Pathological reflexes: Babinski sign on the left. Meningeal symptoms: no stiff neck, Kernig sign was 85 є on both sides. NIHSS score (Stroke Scale of the National Institute of Health,

USA) – 15 points, Glasgow coma scale score – 15 points, modified functional independence Rankin scale score– 4 points.

Past medical history: The patient denies the chronic diseases, hypertension, diabetes, stomach ulcer, myocardial infarction and stroke. Allergies: none. Social history: Smoking during a long time (from adolescence), recently – one pack a day. Alcohol using: occasionally.

Neurologist was set preliminary diagnosis: Acute stroke in the right hemisphere. Conclusion resuscitation: Vital function's violations not noted.

Laboratory studies were appointed emergency: 1. Computed tomography (CT) of the brain; 2. Blood coagulation: platelets, INR (international normalized time), aPTT (activated partial thromboplastin time), PT (prothrombin time); 3. Echocardiography; 4. Complete blood count; 5. Blood glucose; 6. Electrocardiogram (ECG); 7. Biochemical blood tests; 8. Urine test; 9. Duplex ultrasound study of brachiocephalic vessels, transcranial Doppler scan of cerebral vessels; 10. Chest X-ray.

ECG and blood test sample were performed in the RVS's admission room. ECG conclusion: sinus rhythm, and tachycardia, heart rate 95 beats per minute, vertical electrical axis of the heart. For emergency indications CT study of the brain performed at 14:56. CT imaging showed hyperattenuation of the middle cerebral artery (MCA), fuzzy hypoattenuation in the upper dorsal-frontal divisions, in the middle frontal and precentral gyrus. Conclusion of CT studies: It is not excluded area of acute ischemia in the dorsal-frontal sections of the right hemisphere in the pool right middle cerebral artery.

After CT study patient was admitted to the stroke intensive care unit at 15:15. Results of laboratory tests were received duty neurologist at 15:30. Conclusion of testing: 1. Coagulation: aPTT – 37.6, INR – 1.06, PT – 14.3; 2. Complete blood count: leukocytes – $9.3*10^9$/l, erythrocytes – $4.26 * 10^{12}$/l, hemoglobin – 163 g/l, platelets – 165×10^9/l; 3. Biochemical blood tests: total bilirubin – 11.2; ALT – 28, ASAT – 24, glucose – 6.1 mmol/l.

The cerebral and brachiocephalic vessels ultrasound imaging showed the occlusion of the right internal carotid artery (ICA). Ultrasound imaging conclusion: Signs of stenosis and occlusion of extra-and intracranial sections of brachiocephalic arteries due to combined origin (atherosclerosis and thrombosis) – stenosis of the right ICA (moderate grades), complicated by occlusion ICA (from its beginning to the ophthalmic artery). Signs of development of systemic deficiency blood flow in the right middle cerebral artery (MCA), the lack of collateral compensation flow.

Echocardiogram conclusion: Global left ventricular ejection is normal, fraction of 60%. Violations of local contractility of the left ventricle were not found. Anterior mitral valve is seal slightly. Cavities of the heart are not expanded.

Thus, on the basis of medical history, complaints, clinical, instrumental and laboratory testing clinical diagnosis was established: Ischemic stroke in the right middle cerebral artery (atherothrombotic variant).

The testing of the presence of contraindications for TLT performed according to the methodological manual of the Institute of cerebrovascular disease and stroke (Moscow), 2011 [3]. The procedure contraindications had been not established. Considering the ischemic type of stroke, admission of patient in a 4.5-hour "therapeutic window", preservation of clinical symptoms (severe focal symptoms: NIHSS score 15 points), absence of contraindications the duty neurologist decided to hold systemic thrombolytic therapy. The procedure was carried out with thrombolytic rt-PA Actilyse (alteplase) in a dose of 0.9 mg/kg, with monitoring vital signs (blood pressure, heart rate, respiration rate, body temperature, oxygen saturation), neurological and physical status during the TLT time and during the two days following the procedure. The catheters were installed in the left and right cubital vein before the procedure.

Protocol of the procedure: Patient's weight – 85 kg. The total dose of Actilyse – 76.5 mg.

16:00. Started introduction Actilyse: 7.65 mg intravenously per bolus over 1 minute, then intravenously 68.85 ml during 1 hour. Blood pressure – 174/112 mmHg. Heart rate – 71. Respiration rate – 20. SO_2 – 100%. Body temperature – 36.2 C є. NIHSS – 15 points.

16:15. Blood pressure – 169/112 mmHg. Heart rate – 95. Respiration rate – 18. SO_2 – 95%. NIHSS – 6 points. The positive neurological trend was registered: reduction of motor disorders, the movements in the left extremities appeared.

Neurological status: Consciousness: no lowering. Eye's slits D = S. Pupils were equal and reactive to light. Eyeball's movements were limited to the left. No nystagmus noted. Facial nerve: left corner of the mouth was omitted. The tongue was rough to the left. Left-sided hemiparesis: moderate. Muscle tone in the left extremities was reduced. Tendon reflexes were reduced on the left extremities. Pathological reflexes were not noted. Sensitivity: hypoesthesia in the left extremities. Speech disorders: dysarthria. Meningeal symptoms: no stiff neck, Kernig sign was 85 є on both sides.

16:30. Blood pressure – 183/105 mmHg. Heart rate – 85. Respiration rate – 18. SO_2 - 95%. NIHSS – 3 points. Dynamic of neurological status: Left-sided hemiparesis had reduced. Strength in the left extremities: 4.5 points. Sensory disorders had regressed.

16:45. Blood pressure – 179/125 mmHg. Heart rate – 90. Respiration rate – 18. SO_2 – 94%. NIHSS – 3 points. Dynamic of neurological status: Gaze paresis had regressed. Eyeball's movements were full. Slight left-sided hemiparesis, speech disorders (dysarthria) were observed.

17:00. Thrombolysis was over. Blood pressure – 172/106 mmHg. Heart rate – 64.

Respiration rate – 18. SO_2 – 97%. Body temperature – 36.6 C є.

Patient received the procedure satisfactory. The positive dynamic changes were registered: Gaze paresis had regressed. The movements had appeared in the left extremities. Left-sided hemiparesis regressed to 4.5 points. Following neurological disorders stored: slight hemiparesis (4.5 points) and dysarthria. NIHSS score – 2 points.

The cerebral and brachiocephalic vessels ultrasound imaging registered the reperfusion in right MCA (M1, M2), and signs of collateral compensation through the posterior communicating artery and the functioning of the eye anastomosis.

17:10. Blood pressure – 184/104 mmHg. Heart rate – 84. Respiration rate – 18. SO_2– 98%. CT brain imaging was performed for excluding TLT bleeding complications. No signs of hemorrhagic transformation were observed. CT conclusion: It is not excluded there is acute ischemia in the dorsal-frontal regions of the right hemisphere in the pool right MCA.

CT brain imaging performed after one day from the illness onset, it diagnosed ischemic cerebral infarction. CT conclusion (05/11/12): Ischemic stroke in the pool right MCA, the second stage of evolution.

Medications:the neuroprotective therapy appointed immediately after TLT, the anticoagulation appointed 24 hours later. Vital signs monitoring, neurological and somatic status was performed in stroke intensive care unit during the two days. Then the patient was transferred to the RVC's neurological stroke department to continue treatment and neurorehabilitation. Cardiologist, vascular surgeon, ophthalmologist examined the patient. The treatment (antiplatelet and neuroprotective therapy, physiotherapy, massage, speech therapy sessions, occupational therapy, psychological testing) had given positive trend: regression of motor disorders (to full strength in the left extremities), hemodynamic stabilization.

Hospital discharge physical examination: Skin and visible mucous: clean and normal color. Lungs: clear to auscultation. Heart: regular rate and rhythm. Blood pressure – 120/80 mm Hg. Pulse was 75. The abdomen is soft and painless on palpation. Physiological functions are not violated. Neurological status: Pupils were equal. Eyeball's movements were full. No nystagmus noted. Facial nerve: left nasolabial fold smoothed slightly. The tongue was without deviation. No speech disorders noted. Positive symptoms of oral automatism noted. No extremity's paresis noted. No sensory disorders noted. Coordination tests performed satisfactorily. Meningeal signs were not observed. NIHSS store – 1 point, Glasgow Coma Scale – 15 points, Rankin scale – 1 point, Rivermid scale – 14 points.

The patient was discharged from hospital at November 19, 2012. Diagnosis: Ischemic stroke in the pool right middle cerebral artery (from 11/04/12.), atherothrombotic type. Cerebral and

brachiocephalic artery's arteriosclerosis. Occlusion of the right internal carotid artery. State after systemic thrombolysis (11.04.12). Hemorrhagic transformation 0.

Recommendations: monitoring of blood pressure daily; no smoking and alcohol consumption; diet with restriction of animal fats; and chronic antiplatelet therapy.

Conclusions. This clinical report illustrates the effectiveness of systemic thrombolytic therapy with rt-PA in patients with initial severe neurological deficits (hemiplegia, hypoesthesia, dysarthria, gaze paresis (NIHSS score 15 points)). Positive neurological changes was observed on 15 minutes after TLT beginning – movements appeared in the left extremities, followed reduction of the degree of paresis and sensory disorders, regression of contralateral eye paresis. There were "dramatic" decrease of focal symptoms (NIHSS score 2 points) after TLT, it led to the full recovery of lost function and to the independence of the patient's daily life (modified Rankin scale score – 1 point). Clinical improvement occurred against persistent occlusion of internal carotid artery by ultrasound in the dynamics. This phenomenon can be explained by reperfusion in the right middle cerebral artery's system through collateral circulation via the posterior communicating artery and ophthalmic anastomosis. It was confirmed by transcranial Doppler study.

The time from the onset of the first symptoms to the admission in the RVC was 50 minutes, from hospitalization to the first CT study – 14 minutes, to the procedure TLT – 78 minutes. In general, the time from onset of symptoms to the TLT procedure was 2 hours 08 minutes. Thus, thrombolytic therapy was performed to the patient in the first hours after illness onset, during the so-called "therapeutic window". The time factor is very important for the success of thrombolytic therapy. The longer period before perfusion likely results the less of the rapid normalization of microcirculation in the ischemic zone and results the higher risk of additional reperfusion injury and hemorrhagic complications [2].

Thus, systemic thrombolytic therapy can significantly reduce the degree of neurological deficit and improve outcome in patients with ischemic stroke. In Yakutia the number of performed procedures and the result of reperfusion therapy in ischemic stroke will depend from the timely and coordinated work of many pre-hospital and hospital specialists, and from the degree of public awareness about the first signs of a stroke. Another important objective is the introduction of new reperfusion methods in ischemic stroke, including intra-arterial thrombolysis, mechanical clot extraction and combined thrombolytic therapy, in Regional Vascular Center.

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