Cerebrospinal and commissural diaschisis in acute stroke patients: case study

Abstract. Background. Stroke remains the second leading cause of disability and death with the highest reported age-standardized death rates in Eastern Europe compared to Western Europe and the US. Recovery from stroke has been shown to involve reorganization in motor and premotor cortical areas. The resolution of diaschisis has been suggested as a mechanism of early spontaneous recovery. However, there are not enough published prospective studies on the clinical analysis and comparison of different types of cerebral diaschisis, especially in acute stroke patients. We aimed to carry out follow-up analysis of clinical characteristics of cerebrospinal and commissural cerebral diaschisis in acute ischemic stroke patients, to present clinical cases. Materials and methods. We have conducted a prospective, hospital-based, cohort study of acute stroke patients (n = 124) who were admitted to the department of cerebrovascular diseases of the University Hospital (Oleksandrivska Clinical Hospital, Kyiv, Ukraine) within the first 24 hours after the stroke. All cases were reviewed by at least two board-certified neurologists trained in cerebrovascular diseases. All participants underwent comprehensive clinical, neurological, laboratory, ultrasound, and neuroimaging examination. Results. Among 124 patients, 26 were diagnosed with cerebral diaschisis (cerebrospinal (n = 22) and commissural (n = 4)). We have provided detailed clinical analysis of cerebral diaschisis in acute stroke patients. We have described specific neurological changes in variants of territorial cerebral infarctions and mirror brain infarctions caused by diaschisis. Conclusions. Semiotics of acute cerebral stroke is determined, not only by the primary brain infarction, but also by the diaschisis that causes more severe neurological deficit. Cerebral diaschisis is associated with the mirror brain infarction development, depression of tendon and periosteal reflexes, limb muscle atony. During therapy, a sluggish stage of hemiplegia in most cases was followed by the spastic hemiplegia within 9 to 14 days after stroke development. Keywords: diaschisis; cerebral diaschisis; cerebrospinal diaschisis; commissural diaschisis; clinical features; stroke; acute ischemic stroke; case; case report

Introduction

Stroke remains the second leading cause of death among people over 60 and the fifth leading cause of death in people aged 15 to 59 years [1–7]. Annually, 15 million people worldwide suffer a stroke [8–10]. Of these, 5 million die and another 5 million are left permanently disabled, placing a burden on family and community [11, 12]. In the US, a stroke occurs about every 40 seconds and kills someone about every 3 minutes [13]. Death rates from strokes are generally higher in Central and Eastern Europe than in Northern, Southern and Western Europe [14–17]. The highest reported age-standardized stroke death rates (1980 to 2015) are in Kazakhstan, Romania, and Ukraine [18–22]. These rates are 3 to 4.5 times higher than in Western Europe. According to the International Multicenter Research Report (2015), the incidence of stroke continues to increase while the age of stroke victims continues to decrease [23–25].
Recovery from stroke has been shown to involve reorganization in motor and premotor cortical areas [26, 27]. In 1914, Constantin von Monakow developed the concept of diaschisis as a principle for recovery in brain lesions [28–30]. In diaschisis (i.e., dysfunction of brain structures in other vascular areas that are functionally linked to the damaged region, caused by the imbalance of inhibitory or excitatory neurotransmission), restoration of function is associated with the elimination of neural depression of sites, which are remote from the zone of injury, but related to it [31–35]. These depressive changes are usually expressed as a decrease in metabolism, blood flow, or neurotransmitter function [36] similar to transient ischemic attacks [37–39]. Resolution of diaschisis has been suggested as a possible mechanism of early spontaneous recovery for at least a century [40]. While resolution of diaschisis plays a significant role in stroke studies, there are not enough published scientific papers (including Ukrainian scientific literature) devoted to the analysis of the neurological clinical features caused by the impact of the primary focus of stroke with combined (or sequential) effect of the diaschisis phenomenon on the structures of brain damage that form a common neurological deficit often leading to patient’s disability.

Purpose: clinical analysis of cerebrospinal and commissural cerebral diaschisis (analysis of clinical cases) in a prospective, hospital-based, cohort study of acute ischemic stroke patients.

Materials and methods

The methods of the study have been reported in detail previously [27, 41]. A prospective, hospital-based, cohort study was carried out in acute ischemic stroke patients with diaschisis who were admitted to the department of cerebrovascular diseases. All patients in this study were admitted to the department of cerebrovascular diseases of the University Hospital (Oleksandrivska Clinical Hospital, Kyiv) within the first 24 hours after the stroke and were examined by an on-call neurologist. Upon arrival, a detailed medical history was obtained, and medical records were reviewed to exclude previous strokes, transient ischemic attacks. If a prior stroke/transient ischemic attack was reported, clinical data and ancillary study results (e.g., brain imaging) were requested from the treating hospital or practitioner. All cases were reviewed by at least one additional board-certified neurologist trained in cerebrovascular diseases, and were evaluated daily, during the period of patient’s hospitalization.

Stroke was defined according to the World Health Organization and American Heart Association criteria [42, 43]. The etiology of stroke was classified according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria [44]. We used the National Institutes of Health Stroke Scale, modified Rankin scale, and the Barthel index for all patients based on the data available upon arrival and in their medical records [45].

Patients underwent a standardized examination to obtain clinical history: 12-lead electrocardiogram, blood testing (blood chemistry, thyroid, renal, and hepatic function, complete blood count, serum glucose, coagulation studies), carotid Doppler ultrasound (carotid duplex (Multigon 500M, USA) or carotid triplex (Aloka SSD-4000, Japan) scan, head computed tomography (Toshiba Aquilion 16 MultiSlice CT system, Nasu, Japan) and 1.5T brain magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) (Vantage MRI System, Japan) within 24–72 hours after the onset of symptoms and in dynamics, during the period of maximum severity of symptoms. Patients with clinical contraindications to MRI and MRA were excluded from this study. A chest radiograph was done if pulmonary disease or heart failure were suspected.

Stroke treatment and secondary stroke prevention were prescribed according to the American Heart Association/American Stroke Association and European Stroke Organization Guidelines immediately after the diagnosis of stroke [15, 46–52].

Parametric and nonparametric univariate comparisons were performed with $\chi^2$, Fisher’s exact, Mann–Whitney U, and Student’s t tests, as appropriate. A two-sided $p < 0.05$ was considered significant for all analyses. All statistical analyses were performed using IBM SPSS Statistics Version 22 (IBM, Armonk, NY).

Results and discussion

Basic characteristics of study population

In total, 124 patients aged 28 to 84 years with acute ischemic stroke were screened. The distribution was as follows: 68 patients were diagnosed with stroke in the cerebral hemispheres, 11 developed stroke in brainstem, in 45 persons, cerebellar stroke was detected. All stroke localizations were confirmed by neuroimaging. Among 124 patients, 52 individuals had no clinical contraindications for MRI, agreed to participate in the study and were included for the primary analyses and follow-up forming our study group (32 men and 20 women with mean age 58.9 ± 11.6 years). According to the TOAST criteria, the atherothrombotic subtype of stroke was diagnosed in 32 patients and cardioembolic — in 20.

Based on the localization of the primary brain lesions foci and considering secondary dysfunction of brain neighboring structures, we have analyzed and described specific clinical characteristics and manifestations of two forms of cerebral diaschisis: cerebrospinal (n = 22) and commissural (n = 4).

Clinical analysis of cerebrospinal and commissural cerebral diaschisis

Cerebrospinal diaschisis occurred in 22 patients after acute ischemic stroke in the carotid bed that developed as a result of embolism of large and medium caliber cerebral vessels due to atherothrombosis and cardioembolism: 12 persons were diagnosed with internal carotid artery thrombosis in the extracranial part, 7 had embolic obstruction of the main trunk of the middle cerebral artery (MCA), and 3 patients had a lesion in the area of deep branches of MCA.

Thrombosis of internal carotid artery at the site of atherosclerotic lesion and embolic occlusion of MCA, confirmed by the Doppler method, led to the development of a total anterolateral stroke that is a type of a territorial cerebral infarction.
According to the clinical course, these were forms of ischemic impairment of cerebral circulation with an acute sudden onset of stroke symptoms, manifested with contralateral hemiplegia, total hemianesthesia, and hemianopsia; gaze paresis and speech disorders were also observed. If a lesion localized in the left hemisphere of the brain, disorders of the body scheme were detected in patients with infarction of the right brain hemisphere. All patients exhibited symptoms such as depression of tendon and periosteal reflexes, atony of paretic limb muscles, caused, according to von Monakow theory, by “paralysis” of the motor cells of the anterior horns of the spinal cord that connected to the damaged area of the cerebral cortex by the anatomical system of conducting pathways.

During therapy, a sluggish stage of hemiplegia was followed by the spastic hemiplegia at different times after the stroke development: in 9 patients, sluggish stage of hemiplegia occurred within 5–7 days of stroke treatment; in 10 persons — within 8–14 days; and in 3 patients, diaschisis persisted and the spastic hemiplegia didn’t occur (such cases von Monakow interpreted as a “frozen diaschisis”). The duration of the sluggish stage of hemiplegia was determined by various factors: the volume of the brain infarction foci, the severity of the stroke, the age of the patient and concomitant somatic diseases.

The commissural diaschisis (in 4 patients) developed as a result of a partial brain infarction in the left carotid bed, caused by cardioembolic (3 cases) and arterio-arterial embolism from atheromatous arteries (1 case), and manifested itself within 16 hours to 3 days after the onset of the primary brain lesion.

As a result of cortical infarction in the left hemisphere of the brain, the function associated with it, via commissural fibers of symmetric regions of the opposite hemisphere, was disturbed [30]. Perfusion impairment manifested in a change in the average blood flow in the middle cerebral artery, not only on the side of the brain lesion foci (ipsilateral) (31.3 ± 3.7 cm/s), but also on the opposite (contralateral) side (38.0 ± 2.0 cm/s). Hypoperfusion and associated neuronal metabolism dysfunction led to the development of a new focus of brain ischemia in the opposite brain hemisphere, similar to the primary foci of ischemic lesion by the typical characteristics, but different in size, called a mirror infarction.

The mirror infarction occurred mainly in the zones of adjacent blood supply of anterior cerebral artery (ACA), MCA and posterior cerebral artery (PCA) [27, 53–56] and was caused by a sudden loss of interhemispheric connections, i.e., commissural diaschisis, which led to the hypoperfusion in the hemisphere opposite to the primary ischemic lesion brain hemisphere. Primary neurologic symptoms of the mirror brain infarction were determined by its localization: in the ACA — dysphasia, pseudodementia behavior, asymmetrical paresis in the distal legs, grasping reflex; in the adjacent areas of ACA and MCA — the posture of “a man in a barrel” manifest itself in by the paresis of both arms and preserved normal strength of legs; in the adjacent zones of blood supply to MCA and PCA — in bilateral vision impairment, gnosia, praxis.

Conclusions

Clinical analysis of the features of neurological disorders and effective neuroimaging methods in patients with cerebrospinal and commissural cerebral diaschisis showed that semiotics of acute cerebral stroke was determined not only by the primary brain lesion foci (infarction), but also by the universally recognized phenomenon of diaschisis of one or another level of the central nervous system, which is connected with the affected area of the brain via system of conducting pathways. Simultaneous or sequential damage to the anatomically and functionally related sites of neighboring brain structures caused more severe neurologic deficit.

The key to the understanding of ischemic damage in anatomically and functionally related brain formations of different levels, following a cerebral stroke, is described in von Monakow doctrine of diaschisis. This doctrine allows clinicians to understand the pathophysiological mechanisms and to verify specific symptoms, which appear after an acute hemispheric stroke on the side of the central hemiplegia. Such symptoms are: depression of tendon and periosteal reflexes, limb muscle atony, topically similar to the primary lesion in mirror brain infarction.

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Author contributions

S.M. Vinychuk — study concept and design, interpretation of data, data acquisition.

0.Ye. Fartushna — article concept and design, literature overview, data acquisition, interpretation of data, and drafting the article.

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Мы провели проспективное исследование, в котором участвовали 124 пациента (в том числе 22 с цереброспинальным и 124 с комиссуральным диашизом), поступивших в отделение цереброваскулярных заболеваний Университетской больницы (Александровская клиническая больница, г. Киев, Украина) в течение первых 24 часов после развития инсульта. Всё это позволило нам провести клинический анализ различных вариантов церебрального диашиза.

Цель исследования: динамический анализ клинических проявлений цереброспинального и комиссиурального вариантов диашиза у пациентов с острым инсультом.

Резюме. Актуальность. Инсульт остается второй основной причинной инвалидности и смертности с самыми высокими показателями заболеваемости и летальности в странах Восточной Европы по сравнению с Западной Европой и США. Ранее восстановление неврологических функций после инсульта связано с реорганизацией в моторных и премоторных участках коры головного мозга и объясняется феноменом диашиза, особенно у пациентов с острым ишемическим инсультом.

Результаты. Среди 124 обследованных с острым инсультом церебральный диашиз был диагностирован у 26 пациентов (цереброспинальный (n = 22) и комиссуральный (n = 4)). Основные клинические проявления диашиза включают двигательные расстройства, судороги, нарушение чувствительности и симптомы сосудистого криза.

Анализ клинических случаев. У всех пациентов с церебральным диашизом отмечались двигательные аномалии, такие как асимметрия волевого контроля, нарушение координации движений, хорея и атаксия. У пациентов с комиссиуральным диашизом преимущественно наблюдалась асимилиация, то есть совпадение двигательных реакций в доминантной и не доминантной руках.

Оригинальное исследование. /Original Researches/

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Цереброспінальний та комісуральний діашиз у пацієнтів із гострим інсультом: аналіз клінічних випадків

Резюме. Актуальність. Інсульт залишається другою основною причиною інвалідності та смертності з найвищими показниками захворюваності та летальності в країнах Східної Європи порівняно з Заходньою Європою та США. Раннє відновлення неврологічних функцій після інсульту пов’язане з реорганізацією в моторних і премоторних ділянках кори головного мозку та пояснюється феноменом діашизу. Проте на сьогодні опубліковано недостатньо проспективних досліджень щодо клінічного аналізу та порівняння різних варіантів церебрального діашизу, особливо в пацієнтів із гострим ішемічним інсультом. Мета дослідження: динамічний аналіз клінічних проявів цереброспінального та комісурального варіантів церебрального діашизу в пацієнтів із гострим ішемічним інсультом на основі презентації клінічних випадків. Матеріали та методи. Ми провели проспективне госпітальне когортне дослідження хворих на гострий інсульт (n = 124), які надійшли до відділення цереброваскулярних захворювань Університетської лікарні (Олександрівська клінічна лікарня, м. Київ, Україна) протягом перших 24 годин після розвитку інсульту. Під час госпіталізації всі пацієнти пройшли комплексне клініко-неврологічне, лабораторне, ультразвукове та нейровізуальне обстеження.

Результати. Серед 124 обстежених із гострим інсультом церебральний діашиз було діагностовано в 26 пацієнтів (цереброспінальний (n = 22) та комісуральний (n = 4)). Ми провели детальний клінічний аналіз проявів мозкового діашизу. Описано специфічні неврологічні зміни територіальних інфарктів мозку та дзеркальних інсультів, викликаних діашизом. Висновки. Семіотика гострого церебрального інсульту визначається не тільки первинним інфарктом мозку, але й діашизом, що обумовлює більш серйозний неврологічний дефіцит. Церебральний діашиз пов’язаний з розвитком дзеркальних інфарктів мозку, пригніченням сухожильних та територіальних рефлексів, атонією м’язів кінцівок.

Ключові слова: діашиз; церебральний діашиз; цереброспінальний діашиз; комісуральний діашиз; клінічні ознаки; інсульт; гострий ішемічний інсульт; клінічний випадок