Clinical vascular syndromes of thalamic strokes in anterior and paramedian vascular territories: a prospective hospital-based cohort study

Abstract. Background. The article covers pathophysiological features and patterns of the occurrence of neurological, neuropsychological, and clinical vascular syndromes of thalamic strokes in anterior and paramedian vascular territories. The features of neurological clinical picture, topical, and neuroimaging diagnosis of thalamic strokes in anterior and paramedian vascular territories are analyzed and described. We purposed to describe and analyze the clinical and neuroimaging features of vascular syndromes of thalamic strokes in anterior and paramedian vascular territories in a prospective hospital-based cohort study. Materials and methods. We have prospectively recruited 319 acute stroke patients, admitted within 24 hours from the onset of the stroke symptoms to the Neurological Center at an academic hospital (Oleksandrivska Clinical Hospital) in Kyiv, Ukraine. Comprehensive neurological, clinical, laboratory, ultrasound, and neuroimaging examinations were performed to all patients. Results. MRI/CT-proven thalamic stroke was diagnosed in 34 (10.6 %) of 319 patients, forming a study group. Twenty-two of 34 patients (average age 61.9 ± 10.2 years) were diagnosed with an acute isolated ischemic thalamic infarction, and 12 patients (average age 59.0 ± 9.6 years) were diagnosed with an acute thalamic hemorrhage. Conclusions. Specific neurological features of clinical vascular syndromes of acute thalamic strokes in anterior and paramedian vascular territories were analyzed, compared, and described. Keywords: thalamus; stroke; thalamic stroke; clinical features; syndrome; vascular territory; anterior vascular territory; paramedian vascular territory

Background

Worldwide, stroke is the second leading global cause of death, accounting for 11.8 % of total deaths [1–17]. According to the World Health Organization, 15 million people suffer from stroke each year. Of these, 5 million die and another 5 million are permanently disabled [10, 18, 19]. In addition, more young people are affected by stroke in low- and middle-income countries. On average, stroke occurs 15 years earlier causes more deaths in people living in low- and middle-income countries, when compared to those in high-income countries [8, 20–22].

The thalamus plays an important role in different brain functions including memory, emotions, sleep-wake cycle, executive functions, mediating general cortical alerting responses, processing of sensory (including taste, somatosensory, visual, and auditory) information and relaying it to the cortex, and sensorimotor control [23]. Thalamic stroke, both alone and in combination with infarcts involving other structures, is not rare, accounting for approximately 11 to 23–25 % of cases of all posterior circulation strokes, especially in combination with damage to other structures [24, 25]. However, currently, there are not enough published prospective hospital-based co-
hrot studies that report and analyze pathophysiolog-ical features and patterns of the occurrence of neurological, neuropsychological, and clinical vascular syndromes of the thalamic strokes in anterior and paramedian vascular territories, and their topical diagnosis using clinical, neurological, and neuroimaging methods in a prospective hospital-based cohort study [25–31].

Neurological and neuropsychological symptoms of thalamic strokes are invariably investigated by doctors during an objective examination of the patient, being an integral part of establishing a syndromological, topical, and clinical diagnosis. An analysis of the description of the clinical manifestations of thalamic vascular syndromes in a historical aspect, an assessment of the pathophysiology, features and patterns of the occurrence of certain stroke syndromes in different vascular territories are important for a better understanding of a disease. The determination of vascular thalamic syndrome allows solving two main issues: the presence of damage to a specific vascular territory and a topical diagnosis of the central nervous system damage (thalamic stroke) [30]. Given all this, we performed a comprehensive clinical and neuroimaging analysis of the treatment results and assessed the outcomes of the disease in 34 patients with thalamic stroke, among whom 22 patients had isolated thalamic infarction and 12 — hemorrhage in the thalamus.

The purpose of this study is to describe and analyze the clinical and neuroimaging features of vascular syndromes of thalamic strokes in anterior and paramedian vascular territories in a prospective hospital-based cohort study, providing a comprehensive clinical and neuroimaging analysis.

Materials and methods

The materials and methods of this prospective hospital-based cohort study of acute ischemic stroke patients were reported previously [29–31]. Briefly, from 2001 to 2011 all study participants were admitted to the Neurological Center of Oleksandrivska Clinical Hospital (Kyiv, Ukraine) that consists of an admission department, clinical department of neurology, department of cerebrovascular pathology with intensive care/stroke unit, and a research department of neurology. Patients were admitted to the hospital within the first 24 hours since the first stroke symptoms occurred. All stroke cases were reviewed by at least two board-certified neurologists trained in cerebrovascular diseases. Clinical history, 12-lead electrocardiogram, blood testing, carotid ultrasound, head computed tomography (CT) and/or brain magnetic resonance imaging (MRI) were obtained for all study participants. Stroke was defined according to criteria of the World Health Organization, American Heart Association/American Stroke Association guidelines for adult stroke, and was confirmed by neuroimaging [32, 33]. The etiology of stroke was classified according to the TOAST criteria [34]. The National Institutes of Health Stroke Scale, the Modified Rankin Scale, the Barthel index, and the Charlson Comorbidity Index were determined for all participants. Secondary stroke prevention was prescribed according to the American Heart Association/American Stroke Association and the European Stroke Organisation guidelines immediately after the stroke diagnosis was made [35–41]. Stroke education programs were provided to all study participants [11, 16, 30, 42–45]. Parametric and non-parametric statistic methods were applied. The log-rank test was used for univariate comparisons of event-free survival between groups. A two-sided p < 0.05 was considered significant for all analyses. All statistical analyses were performed using IBM SPSS Statistics Version 22.

Results and discussion

In total, 319 adult patients with acute MRI/CT-proven stroke were screened. Among them, 204 (63.9 %) patients were diagnosed with an acute posterior circulation ischemic stroke, and 115 (36.1 %) individuals had an intracerebral hemorrhage. Thalamic stroke was diagnosed in 34 (10.6 %) of 319 patients, forming the study group. The distribution by stroke type in the study group was as follows:

— 22 patients (12 men, 10 women aged 50 to 84 years; average age 61.9 ± 10.2 years) were diagnosed with an acute isolated thalamic stroke;

— 12 patients (5 men, 7 women aged 57 to 75 years; average age 59.0 ± 9.6 years) had a proven diagnosis of thalamic hemorrhage.

Seven (31.8 %) of 22 patients with isolated thalamic stroke were diagnosed with lesions of small arteries, or lacunar stroke (focal diameter ≤ 1.5 cm), with the typical risk factors background (arterial hypertension, diabetes mellitus) and absence of stenosis of large arteries and a potential source of cardioembolism. Lacunar thalamic infarction was more often determined in the posterolateral adjacent zone (in 5 patients) and in the inferolateral classic vascular territories of the thalamus (in 2 patients).

Non-lacunar stroke with a diameter of foci lesion > 1.5 cm was detected in 15 (68.2 %) patients. It arose as a result of occlusion of the thalamic arteries, branches of the posterior cerebral artery. Ischemic damage to the thalamus in 4 (18.2 %) patients was due to cardioembolism (hypokinesia after myocardial infarction in two cases, atrial fibrillation in one case, pathology of the heart valves in one case); 11 (50.8 %) individuals were diagnosed with atherosclerotic intracranial subtype of ischemic stroke. Non-lacunar thalamic infarcts were mainly localized in the classic thalamic territories (in 11 patients), less often — in the border vascular zones (in 4 people).

In 9 (40.9 %) of 22 patients with isolated thalamic stroke, the lesion was localized in the right thalamus, in 12 (54.5 %) — in the left thalamus, and in one (4.6 %) case, a bilateral lesion of the thalamus was detected. In 15 (68.2 %) patients, foci of lesion were found in the classic vascular thalamic territories (paramedian and lower lateral), in 7 (31.8 %) cases, foci of lesion were detected in the borderline vascular territories (central and posterolateral).

Thus, according to the thalamic stroke localization in the examined patients, four vascular and anatomical terri-
Clinical vascular syndromes of thalamic strokes in paramedian vascular territory

Unilateral stroke of the paramedian vascular territory clinically manifested itself in posteromedian thalamic syndrome. The main symptoms of the syndrome were impaired consciousness, memory, vertical gaze palsy, pronounced neuropsychological disorders, and psychosensory disorders — hallucinosis. It is believed that the depression of consciousness is a result of damage to the posterior parts of the dorsomedial and intralaminar nuclei, as well as a violation of their relationship with the ascending reticular formation and the cerebral cortex [47]. The mechanism of the occurrence of hallucinosis is not fully established. Since the thalamus is an important link of the subcortical–cortical functional loop with feedback, a stroke of the paramedian thalamic territory can generate the excessive impulse to the cortex of the temporal lobe, which is involved in the perception and processing of visual information, which causes the development of hallucinosis [48]. The occurrence of selective impaired upward gaze confirms that paramedian thalamic infarction has a pathological effect on the supranuclear tracts responsible for vertical gaze control without damage to the rostral midbrain [49].

In our study group, paramedian vascular territory (in 6–27.3 % of patients) corresponded to the classic thalamic territory, and the development of a stroke was accompanied by damage to the posteromedian thalamus, including the nucleus of the medial longitudinal fasciculus, the posterior divisions of the dorsomedial and intralaminar nuclei: central, lateral, parafascicular. The development of the posteromedian thalamic syndrome was typical for a unilateral stroke of the paramedian vascular territory, it manifested as an acute depression of consciousness, cognitive impairment, and impaired upward gaze. Clinically, depression of consciousness was detected in all patients: stunning (in 2 patients) manifested itself in a restriction of activity and a slowdown of mental reactions; stupor (in 3 patients) was characterized by a deeper depression of consciousness; one patient with bilateral thalamic infarction was diagnosed with coma with a complete loss of perception of the world and herself. It is believed that the depression of consciousness is a consequence of damage to the posterior parts of the dorsomedial and intralaminar nuclei, as well as a violation of their connection with the ascending reticular formation and cerebral cortex [47].

In most cases, cognitive impairment manifested itself in a memory disorder: in one patient with left-sided lesion of the paramedian vascular territory of the thalamus, retrograde amnesia (loss of memory for events preceding a stroke) was revealed, and in two patients with right-sided damage, anterograde amnesia (loss of memory for events after a stroke) was determined. In one patient with left hemisphere lesion of the paramedian thalamus region, ideomotor and constructional apraxia were detected. In another case with a lesion of the right paramedian vascular territory of the thalamus, anosognosia and ignoring the left half of the space, impaired perceptions of reality in the form of hallucinosis were observed. With left-, right-sided lesions, speech disorders were noted. Vertical gaze palsy was detected in three patients with left-sided paramedian
lesion of the thalamus. A stroke of the paramedian vascular territory of the thalamus also manifested itself in behavioral syndromes — anomie and dysthymia.

**Bilateral stroke of paramedian vascular territory**

More severe neurological dysfunction and symptoms occurred with a *bilateral stroke of paramedian vascular territory*. There is a *paramedian thalamic stroke syndrome* with akinetic mutism, amnestic disorders, which often occur when the dorsomedial nuclei of the thalamus is affected. In our observation, a patient with bilateral paramedian thalamic infarction one year after a stroke developed thalamic dementia, which occurs when the medial dorsal nuclei of the thalamus was damaged along with the mammillary bodies [29, 50]. Bilateral infarction of the paramedian territory occurs due to atheromatous or embolic occlusion of the common branch of the thalamosubthalamic artery known as artery of Percheron.

Resuming, we would like to highlight that unilateral stroke of the paramedian vascular territory of the thalamus manifested itself in posteromedian syndrome (depression of consciousness, vertical gaze palsy, cognitive impairment); more severe symptoms are observed in case of a bilateral stroke (paramedian thalamic infarction syndrome). Moreover, the severe dysfunction of the emotional sphere, such as syndromes of anomie and dysthymia, are revealed in patients with stroke of the paramedian vascular territory of the thalamus.

**Conclusions**

The knowledge of the vascular syndromes of the thalamus was and remains an extremely important component of the supervision of a patient with thalamic stroke, and is an integral part of establishing a topical and clinical diagnosis. It is necessary to continue to analyze clinical observations and the pathology of the nervous system in patients with isolated thalamic infarcts.

**Author contributions**

**S.M. Vynchuk** — study concept and design, statistical analysis, interpretation of data, literature overview, critical revision of the manuscript for important intellectual content; **M.M. Prokopiv** — study concept and design, data acquisition, statistical analysis, interpretation of data, literature overview, critical revision of the manuscript for important intellectual content; **L.M. Trepit** — study design, data acquisition, statistical analysis, interpretation of data; **O.Ye. Fartushna** — study concept and design, literature overview, statistical analysis, interpretation of data, article concept and design, drafting the article, critical revision of the manuscript for important intellectual content.

**Conflicts of interests.** Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

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Резюме. Актуальность. У статті проаналізовано і описано па- тофізіологічні особливості та закономірності виникнення невро- логічних, нейропсихологічних та клінічних синдромів таламічних інсультів переднього та парамедианного судинних басейнів. Вивчаються особливості неврологічної клініки, то- пічної, клінічної і нейровизуалізаційної діагностики таламічних інсультів передньої та парамедианної судинних територій. Мета дослідження: описати і проаналізувати клініко-нейровизуаліза- ційні особливості судинних синдромів таламічних інсультів пе- редньої та парамедианної судинних територій у проспективному клінічному когортному дослідні. Матеріали та методи. Ми провели проспективне клінічне когортне дослідження 319 пацієнтів із гострим інсультом, які надійшли до неврологічного центру Олександріївської клінічної лікарні (м. Київ, Україна) протягом перших 24 годин з моменту розвитку інсульту. Усі пацієнти прошлись комплексне клініко-неврологічне, лабораторне, ультразвукове та нейровизуалізаційне обстеження. Результати. Серед 319 обстежених хворих із гострим інсультом нейровизуалізаційно підтверджений таламічний інсульт діагностовано в 34 (10.6 %) пацієнтів. Із них у 22 особ (середній вік 61.9 ± 10.2 року) виявлено гострій ізольований інфаркт таламуса, а в 12 (середній вік 59.0 ± 9.6 року) — гострій таламічний крововилив. Висновки. Про- аналізовані, порівняні й описані специфічні неврологічні особли- вості клінічних синдромів гострих таламічних інсультів передньої та парамедианної судинних територій.

Ключові слова: таламус; інсульт; таламічний інсульт; клініч- ні особливості; синдром; судинна територія; передня судинна територія; парамедианна судинна територія.