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# A clinical case of migrainous stroke

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**ABSTRACT**

Migrainous stroke is a rare combination of frequently occurring diseases; only a few cases have been described in the domestic literature. The complexity of differential diagnosis is due to the fact that at the stage of initial manifestations, these two conditions can mimic each other. Treatment strategy and further prevention for each of these diseases is different, so timely and convincing early diagnosis is crucial. The presented clinical case describes a case of ischemic stroke in a young woman who had been suffering from migraine for a long time, which did not fully meet the criteria for migrainous infarction. The patient was treated at the regional vascular center of the Tomsk Regional Clinical Hospital, there was a positive trend in the neurological status. The catamnesis of the disease was tracked. It was suggested that endothelial dysfunction is the main pathogenetic factor in the formation of an ischemic focus against the background of a protracted migraine attack.

**Keywords:** migraine, ischemic stroke, migrainous infarction

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# Мигренозный инсульт: клиническое наблюдение

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**РЕЗЮМЕ**

Мигренозный инсульт – это редкое сочетание часто встречающихся заболеваний, в отечественной литературе описаны лишь единичные наблюдения. Сложность дифференциальной диагностики связана с тем,

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что на этапе начальных проявлений эти два состояния могут имитировать друг друга. Лечебная тактика и дальнейшая профилактика при каждом из этих заболеваний различны, поэтому так важна своевременная и убедительная диагностика на ранних этапах.
В представленном клиническом наблюдении описан случай ишемического инсульта у молодой женщины, длительное время страдающей мигренью, который не вполне соответствовал критериям мигренозного инфаркта. Пациентка лечилась в региональном сосудистом центре Томской областной клинической больницы, отмечена положительная динамика в неврологическом статусе. Отслежен катамнез заболевания. Высказано предположение о том, что эндотелиальная дисфункция – основный патогенетический фактор формирования ишемического очага на фоне затянувшегося мигренозного приступа.

**Ключевые слова:** мигрень, ишемический инсульт, мигренозный инфаркт

**Конфликт интересов.** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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## INTRODUCTION

Migrainous ischemic stroke or migrainous infarction (MI) is a rare disease that occurs in the population with a frequency of 1.4–3.4 / 100,000, which is only 0.2–0.5% of all cases of ischemic strokes [1]. According to the brief version of the International Classification of Headache Disorders (ICHD-3 beta, 2013, revised in 2018), this disease under code 1.4.3 refers to complications of migraine [2]. Each of these diseases separately is quite common in the population [1], however, the study of the epidemiology of their combination is quite difficult. This is explained by the fact that before the introduction of clear diagnostic criteria, the diagnosis of MI was vague. Even after their introduction, the establishment of this diagnosis largely depends on the traditions of the clinic and its technical equipment.

The diagnostic criteria for MI are as follows:

A. Migraine attack meets criteria B and C.

B. It occurs in a patient with migraine with aura and a typical previous attack when one or more aura symptoms last > 60 minutes.

C. Neuroimaging shows the presence of ischemic infarction in the corresponding area of the brain.

D. It does not correspond to another diagnosis largely [2].

In other words, MI can be diagnosed only in case of ischemic stroke without another proven cause in patients suffering from migraine with aura at the time of the attack in case of persistent focal neurological symptoms lasting more than an hour and similar to one or more manifestations of the aura, with manifestations characteristic of ischemia on CT or MRI in the corresponding area of the brain. The influence of the following factors on the incidence of MI was proven: female gender, frequency of attacks, smoking, and oral contraceptives with a high content of estrogen [1, 3]. Strokes in patients with migraine that do not occur during an attack are considered only as an associated disease, and not as MI [2]. In real clinical practice, timely and robust diagnosis of MI is still challenging.

## CLINICAL CASE

Female patient F., born in 1969 (50 years old) presented to the Regional Stroke Center (RSC) of the Regional Clinical Hospital on November 27, 2019. She had complaints of tension throbbing headaches (5 points on the Visual Analogue Scale (VAS)) without clear lateralization, nausea, periodic vomiting, awkwardness and left arm numbness. The day before, she was taken to the RSC by an ambulance with complaints of tension throbbing headache (9 points according to the VAS) in the right temporoparietal region, nausea and vomiting, difficulty speaking, which she had for three days. No convincing focal symptoms were found during the neurological exam, computed tomography (CT) of the brain showed no focal changes (Fig. 1).

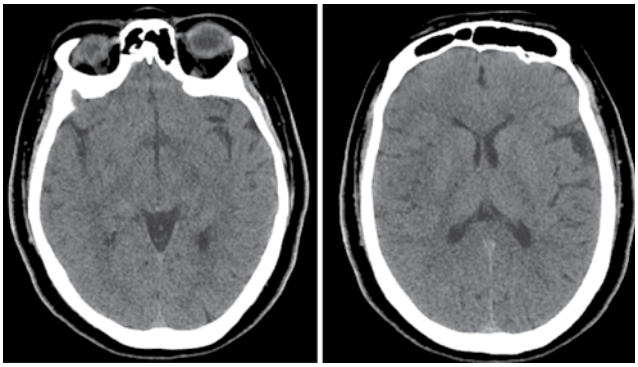


Fig. 1. CT of the brain of patient F. One day before admission to the RSC

With the diagnosis of a protracted migraine attack (simple form), she was referred to a therapeutic hospital on duty. There, the administration of an analgesic (baralgin) eased headache a bit, and the patient was discharged for outpatient follow-up. The next day, moderate diffuse headache and nausea persisted. After sleep, the patient felt left arm numbness and weakness, which was mainly in the hand. Due to her condition, patient's relatives brought her to the RSC again. From the history of present illness, the patient was diagnosed with migraine more than 15 years ago, for 9 years she has been taking sumatriptan (amigrenin), pentalgin, and nise during attacks.

Attacks had the same pattern: a throbbing headache in the right temporoparietal region with nausea and vomiting, a feeling of pressure in the left eye that the patient suffered from 1–2 times a month. The symptoms lasted from several hours to 3 days and could begin spontaneously or be provoked by psycho-emotional stress or odors. When the attack was provoked by odors, the patient had a burning sensation in her nose prior to it. The patient told that drugs, including sumatriptan, did not completely stop the attacks, but sleeping for several hours helped to ease the attack. According to the patient's health history, she suffered from periodic spontaneous vomiting in childhood. The patient had no chronic diseases, except for migraine. She sometimes checked blood pressure, which was not increased. She did not take any medications regularly.

The patient had one pregnancy and one childbirth. Ten years ago, she was operated on for uterine fibroids. For several months, the patient had irregular period. Before admission, she had no period for two months and suspected the onset of menopause. She has not turned not turn to a gynecologist lately and has not taken any hormonal medications. The patient did not smoke. The patient had no family health history of vascular pathology, but her father had similar headaches in his youth.

Upon admission, the neurological examination revealed a slight monoparesis of the left arm; strength was reduced to 4 points, in the hand – up to 3 points, as well as left-sided hemihypesthesia, including the face. A CT scan of the brain on the right in the deep parts of the frontal lobe revealed an ischemic focus 5.0 x 5.0 x 3.5 cm (Fig. 2). With the diagnosis of ischemic stroke in the right middle cerebral artery (unspecified subtype), the patient was hospitalized in the RSC, where an examination was carried out in accordance with the current regulatory documentation (procedure, standard and clinical guidelines).

The results of complete blood count and urinalysis, biochemical blood test, electrolyte test, coagulation test, and lipid profile test were all within the normal range. ECG: sinus rhythm, heart rate 75 beats per minute. The electrical heart axis was horizontal; anterior rotation of the left ventricle around the longitudinal axis of the heart. Daily monitoring of blood pressure revealed no pathology. Echocardiography only revealed minor tricuspid regurgitation. Ultrasound

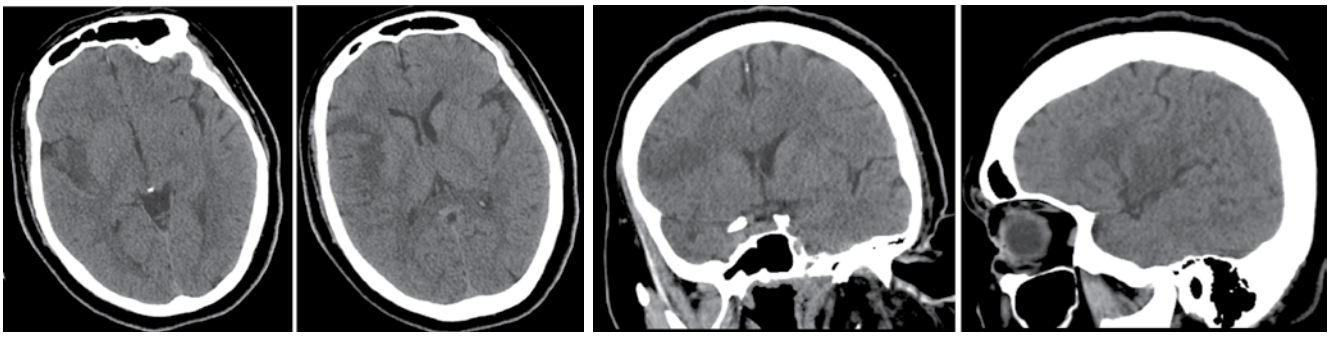


Fig. 2. CT scan of the brain of patient F. at the time of admission to the RSC

examination of extracranial vessels showed asymmetry of the blood flow distribution in the carotid and vertebral arteries. Blood flow deficiency was detected in the right carotid artery and in the left vertebral artery. There was increased peripheral resistance in the system of carotid arteries on the right and vertebral arteries on both sides. Left vertebral artery had a small diameter. Examination of the fundus revealed slight optic disc swelling in both eyes. Retinal angioplasty in both eyes was of hypertonic type. A dynamic CT scan of the brain was conducted 7 days after admission and revealed the focus of subacute ischemia 5.7 x 3.4 x 3.0 cm on the right in the frontal lobe, in the external capsule (Fig. 3). MRI of the brain on day 10 after admission revealed foci of subacute ischemia on the right (increased T2 signal, T2-FLAIR, DWI): a focus of 51 × 11 mm in the subcortical regions of the frontal and parietal lobes and a focus of 11 × 12 mm in the periventricular (medial) regions of the parietal and occipital lobes. Pathology of intracranial vessels was not revealed (Fig. 4). After the examination, the patient was diagnosed with migrainous ischemic stroke in the right middle cerebral artery, left-sided upper mild monoparesis, hemihypesthesia.

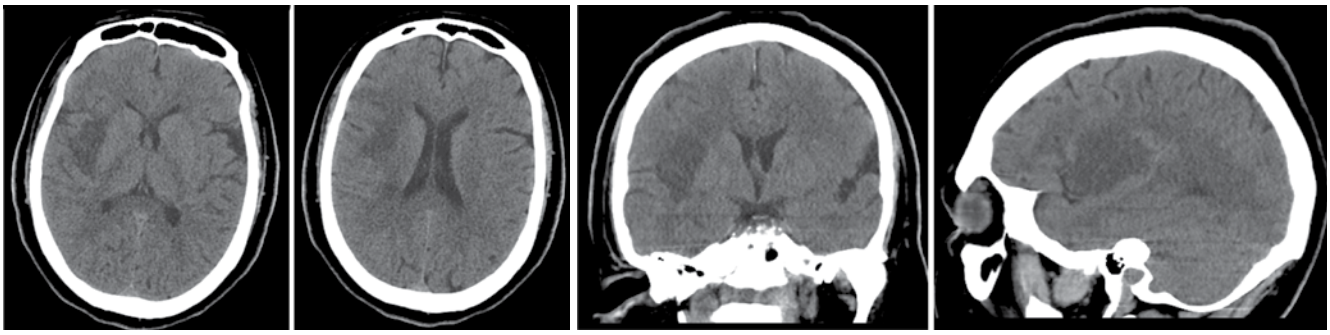
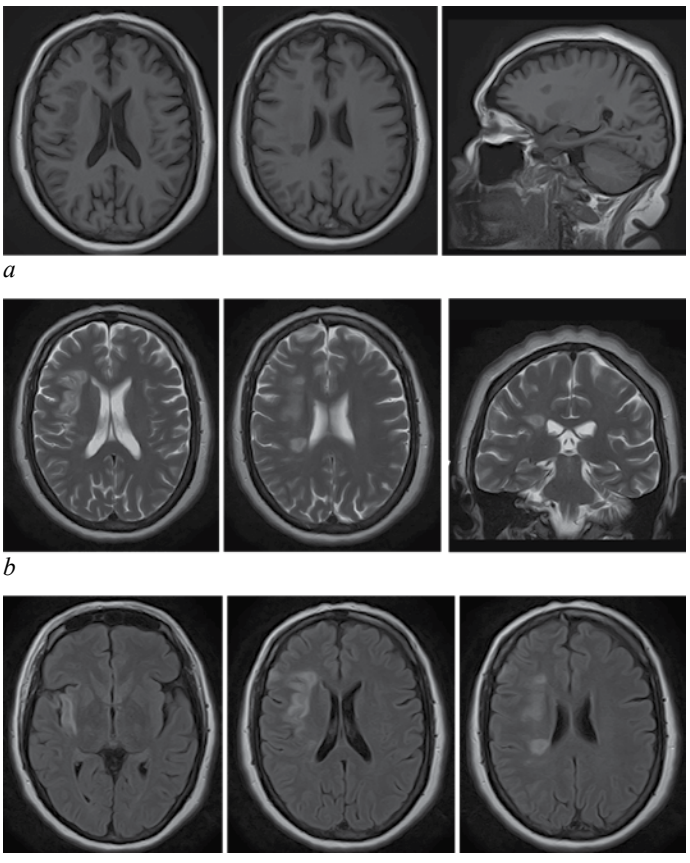


Fig. 3. CT scan of the brain of patient F. 7 days after admission to the RSC



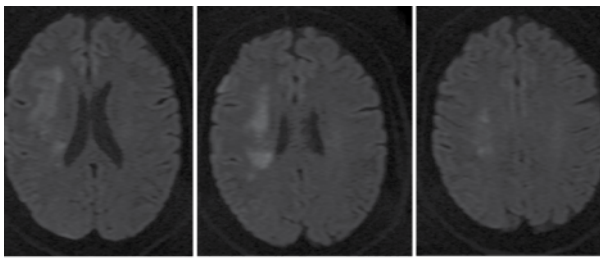
*a*



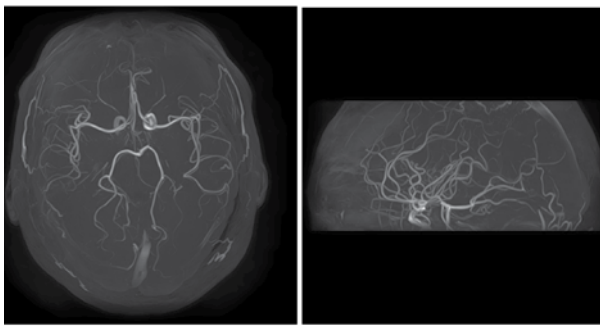
*b*



*c*



*d*



*e*

Fig. 4. MRI of the brain of patient F. 10 days after admission to the RSC. Modes: *a* – T1, *b* – T2, *c* – FLAIR, *d* – DWI, *e* – 3D-TOF

The patient received the following treatment: infusion therapy, citicoline, sulpiride, amitriptyline, acetylsalicylic acid, exercise therapy, physiotherapy, and occupational therapy, and within a few days, strength was restored in the left hand up to 5 points, but awkwardness when moving fingers and hemihypesthesia remained. After the end of treatment, the patient was discharged with positive dynamics in a satisfactory condition for the second stage of rehabilitation at the rehabilitation center. She was recommended to receive a long course of aspirin cardio 100 mg and amitriptyline, a course of citicoline, and sumatriptan for migraine attacks.

Catamnesis was followed up by phone after 2.5 years. After a course of rehabilitation treatment, the neurologic deficit regressed almost completely: sensory disturbances recovered within 8 months, but some awkwardness in the left hand persisted. She also noted some memory loss, which did not affect daily activity. With the onset of menopause and a change of job (she left a managerial position), headaches changed. They became less frequent, no more than once a month, and less intense (5–6 points according to the VAS). The patient did not need to take sumatriptan, as headaches were usually eased by combined NSAIDs (pentalgin) and glycine. She did not take drugs regularly.

## DISCUSSION

The presented clinical case does not fully meet the diagnostic criteria for MI [2]: the patient had no aura. These criteria were formulated based on several meta-analyses, which showed an association of its occurrence with female gender, young age, frequency of attacks, the presence of aura, and the use of oral contraceptives [1, 4–6]. No statistically significant relationship was found between migraine without aura and the risk of ischemic stroke, although such cases were described in both foreign and Russian literature [7]. In addition, it was proven that ischemic foci are more often detected in the posterior circulation and often in the cerebellum [8], while in this case, the ischemic focus was formed in the middle cerebral artery.

According to modern concepts, the activation of serotonergic neurons of the raphe nuclei plays an important role in the onset of a migraine attack. It may initiate a wave of functional inactivation of cortical neurons. This wave of neuronal depolarization, followed by a wave of oligemia, is referred to as “cortical spreading depression”, coincides with the aura phase, and is probably its pathophysiological basis [1].

Endothelial dysfunction may be a common risk factor for both stroke and migraine. The neurovascular effects of endothelial dysfunction ultimately lead to impaired vascular reactivity. Moreover, this is a proven trigger for the activation of procoagulant, proinflammatory, and proliferative mechanisms. In patients with migraine, there is an increase in the activity of key endothelial dysfunction biomarkers: von Willebrand factor, C-reactive protein, nitrate / nitrite levels, as well as circulating endothelial progenitor cells, which correlates with a longer duration of the disease [9]. During a migraine attack, there is an increase in the level of platelet-activating factor, which is released from cerebral endothelial cells, platelets, and mast cells in response to hypoxia possibly induced by cortical spreading depression [10]. It is important that this was found in a study of patients with migraine attacks without aura. Thus, during migraine attacks, a procoagulant state appears which can cause the formation of an ischemic focus.

Probably, in the given clinical case, this was the cause of ischemic stroke in the patient, since its association with a migraine attack is beyond doubt.

## CONCLUSION

The above clinical observation describes a case of migrainous stroke in the deep parts of the cerebral hemisphere in the patient suffering from migraine without aura for a long time during a protracted attack of hemicrania. This does not fully meet the criteria for migrainous infarction because they occur more frequently in women suffering from migraine with aura in the posterior circulation. In this case, we do not have any doubts that migraine caused stroke, while endothelial dysfunction with activation of procoagulant systems during a protracted attack of hemicrania most likely caused the formation of an ischemic focus.

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