

SPECIFIC COURSE OF THE CLINICAL AND NEUROVISUAL FEATURES OF THE CEREBRAL STROKE CAUSED BY REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

Candidate of Medical Sciences, Associate Professor

E.M.Tashkenov

Andijan State Medical Institute.

The aim: to study the specific course of the clinical and neurovisual features of the cerebral stroke caused by reversible cerebral vasoconstriction syndrome (RCVS).

Materials and methods. 30 patients were under our control. The control group consisted of 19 women and 11 men. The age of patients is from 15 to 60 years (the average age (43.3 ± 0.7)). We performed MRI and MR angiographic studies of the brain using the apparatus for MRI "TOSHIBA" (1.5T), conducted USDS of the cerebral vessels, and used the MMSE short mental health assessment scale for an overall assessment of the cognitive system. We used the Reisberg scale (2008) to assess the decrease in overall cognitive activity with an emphasis on memory, the VAS scale to assess the intensity of headaches and the results were statistically processed.

Result: the diagnosis of RCVS (Fleming-Call syndrome) is made on the basis of the patient's clinical picture, the nature of the headache (development speed, headache intensity (100%), nausea (90%)), on the basis of vasoconstriction changes in the brain vessels in an MRI study T1, T2, FLAIR and in blood vessel research modes. In the first group ($n = 23$), there were no focal signs in the brain in the T1, T2, and FLAIR modes; vasoconstriction changes in the cerebral vessels were detected in the MR angiographic. In the second group ($n = 7$), focal changes in the brain were detected in the T1, T2, and FLAIR modes, as well as vasoconstriction changes in the cerebral vessels in the MR angiographic. USDS examination revealed atherosclerotic changes in cerebral vessels in 42% of patients: grade I or II stenosis, and in 58% of patients atherosclerotic changes in cerebral vessels were not detected. **Conclusions:** 1. It has been established that most cases of cerebral stroke caused by RCVS (Fleming-Call syndrome) occur in patients under the age of 55 and are accompanied by high-intensity headaches and vasoconstrictive changes in cerebral vessels.

Key words: Reversible cerebral vasoconstriction syndrome, Fleming-Call syndrome, MR angiography, ultrasound dopplerography.

Introduction - Reversible cerebral vasoconstriction syndrome (RCVS) or Fleming-Call syndrome is a common concept, characterized by acute onset of high-intensity headaches and reversible constrictive changes in cerebral arteries during neurovisual examination [11]. The clinical manifestation of RCVS is a high-intensity headache, which is maximized within a minute, and, as the patient says, it is like a "lightning strike". Headache may be manifested with focal neurological symptoms, or without focal neurological changes, or in combination with convulsive syndrome [8]. There are primary and secondary forms of RCVS. Primary RCVS develops idiopathically, develops faster and relatively earlier, with no cerebral and somatic pathologies, occurs without surgery, without taking vasoactive substances. Primary RCVS occurs in a healthy person under the influence of excitatory factors and do not cause serious complications in patient [7]. It may occur under the influence of the following triggers: during physical activity, sexual activity, severe cough, extreme heat or a cold [9].

Secondary RCVS is manifested as severe vascular pathology. Within 1 - 2 weeks, the patient has a recurrent "thunderclap" headaches", manifested with multifocal vasoconstriction in the cerebral vessels and no other vascular pathology [6]. For example: it occurs when taking vasoactive substances (cannabis, cocaine, ecstasy, amphetamine), ergotamines (ergotamine tartrate, metergin, methylgothamine, lysuride, bromkriptan), sympatomimetics (ephedrine, pseudoephedrine, phenylpropranolamine, isometronone, dethylethanone, serethonerine,

dysregulated drugs) (tryptanes, selective inhibitors of serotonin retention), immunosuppressors (cyclophosphamide, tacrolim), other substances (nicotinic plastic, ginshen, indometacin, hormonal contraceptives, excessive alcohol consumption, erythropoietin, intravenous immunoglobulin, massive transfusion bleeding), during pregnancy, the postpartum period, in pathology or manipulations with extracranial or intracranial blood vessels, in other intracranial diseases or manipulations and under the influence of other factors [1]. Secondary RCVS is not always benign. Complications may occur in: Cerebral edema (38%), transient circulatory disorders in the brain (16%), reversible encephalopathic syndrome (9 - 54%), ischemic stroke (4 - 54%), subarachnoid hemorrhages (34%), intracranial hemorrhage (20%) [12]. After the onset of the first symptom of RCVS, MR angiography may not detect any changes in the blood vessels, and maximal vasoconstriction in the cerebral vessels can be detected 16 days after the initial complaint with repeated MR angiography examination [5]. In MR angiography vasoconstrictive changes of cerebral blood vessels are described as "beads-shaped". The MR angiography is the gold standard in the diagnosis of RCVS[1].

The aim of research: to study the specific course of the clinical and neurovisual features of the cerebral stroke caused by reversible cerebral vasoconstriction syndrome (RCVS).

Materials and Methods: 30 patients were under our control, who were treated in the Neurology department of the clinic of Andijan State Medical Institute and in the Neurology and Resuscitation departments of medical units at the Department of Health. There are 19 women and 11 men. The age of patients is from 15 to 60 years old (the average age (43.3 ± 0.7)). We performed MRI and MR angiographic studies of the brain using the MRI apparatus "TOSHIBA" (1.5T), and used MMSE short mental health assessment scale (28-30 points - norm, 24-27 points - cognitive impairment, 20-23 points - mild dementia, 11-19 points - moderate dementia, 0-10 points - severe dementia), the Reisberg scale (2008) to assess the decrease in overall cognitive activity with an emphasis on memory, the VAS scale to assess the intensity of headaches (0 points - norm, 1-3 - slight pain, 4-6 points - moderate pain, 7-9 - very severe pain, 10 - unbearable pain).

We divided patients into 2 groups. The first group consisting of 23 patients had uncomplicated RCVS, the second group consisting of 7 patients had complicated RCVS. 65% of the first group were women, the rest 35% were men; 57% of the second group were women and 43% were men. (Picture 1).

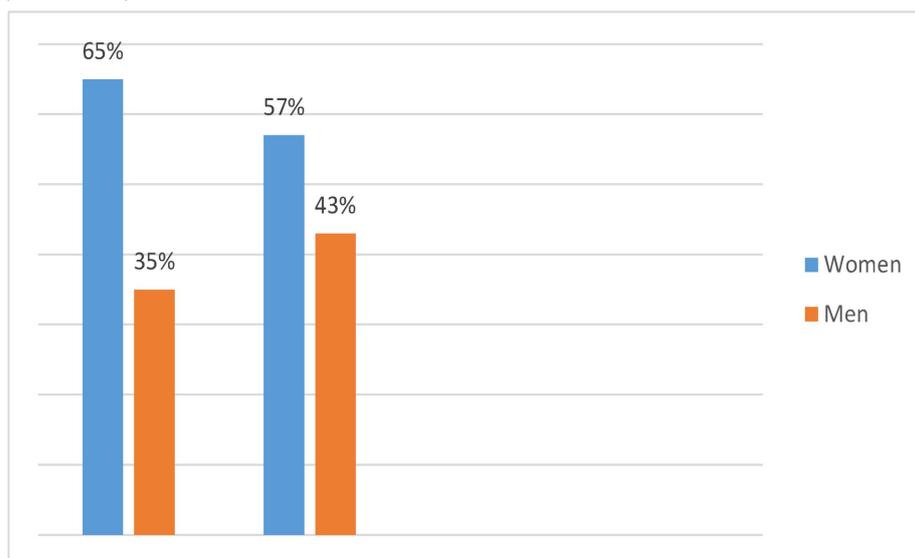


Figure 1. Gender characteristics of patients with reversible cerebral vasoconstriction syndrome (n = 30).

Percentage of patients by age: In the first group, the patients aged 16 to 35 composed 40%, patients aged 36-50 composed 30%, 30% of patients aged 50-70. The second group comprises

14% of patients aged 16-35, 44% of 36-50 years old, and 42% of patients aged 50-60 years (Figure 2).

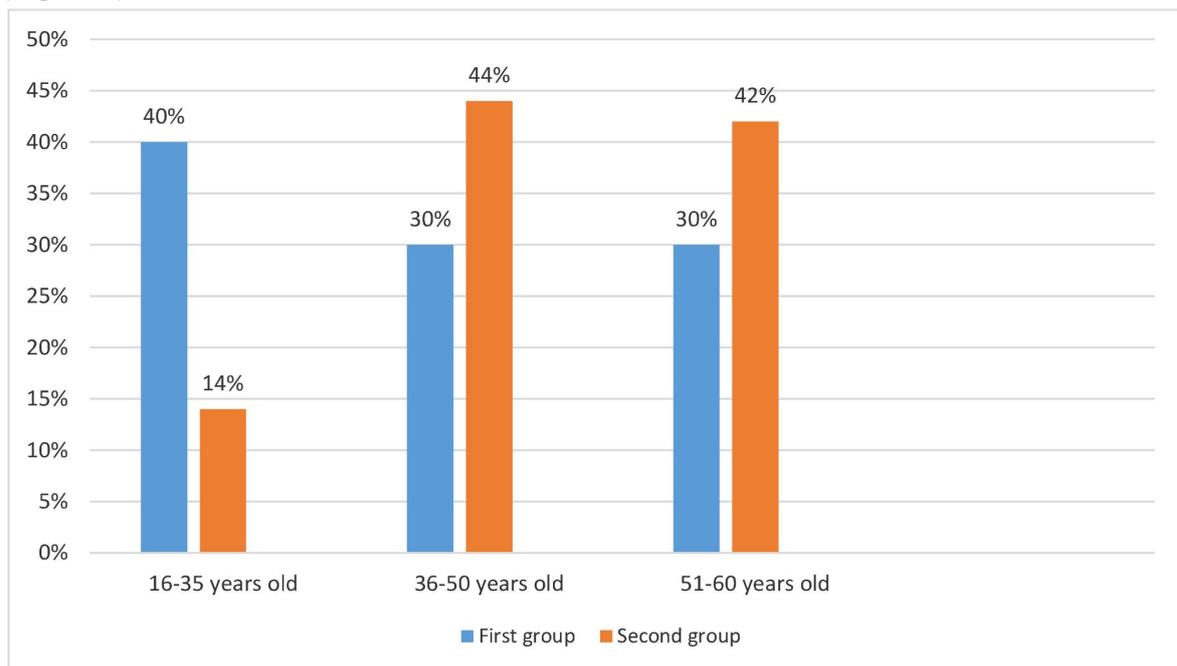


Figure 2. Age distribution of patients with reversible cerebral vasoconstriction syndrome.

Patients in the first group were patients with uncomplicated RCVS (Fleming-Call syndrome); in the second group, we studied the specific complications of RCVS (Fleming-Call syndrome). In the second group of patients ($n = 7$) in 28% hemorrhagic stroke, in 58% ischemic stroke, and in 14% transient circulatory disorders in the brain. Mathematical processing was carried out using the student's method, parametric and non-parametric criteria (Kruskal-Wallis criterion, Mann-Whitney criteria).

Results: the diagnosis of RCVS (Fleming-Call syndrome) is made on the basis of the patient's clinical picture, the nature of headache (development speed, headache intensity (100%), nausea (90%)), suffering from migraine - 83% of patients with migraine history in both groups, on the basis of vasoconstrictive changes in the cerebral vessels in MRI study T1, T2, FLAIR and in MR angiographic. (Table 1). These vasoconstrictive changes persist for 3 months.

Table 1.

Diagnosis of Fleming-Call syndrome.

	The first group	The second group
Complaints, anamnesis	Rapid development of headache, high intensity headache (100%), nausea (80%). In anamnesis, 76% of patients have migraine.	Rapid development of headache, high intensity headache (100%), nausea (80%). In anamnesis, 92% of patients have migraine.
Neurostatus	The absence of focal changes in the brain	The presence of focal changes in the brain
Neuroimaging studies	In T1, T2, FLAIR mode no brain changes were detected in 21.7% patients, 88.9% had hypotrophy in the cerebral cortex, small focal gliosis in the white matter of the cerebral hemispheres, infiltrative changes in subcortical structures and	In T1, T2, FLAIR mode focal changes in the hemispheres of the brain (in 2 patients in the parietal region of the cerebral hemisphere, in 2 in the occipital region, in 2 patients in the upper frontal region, in 1 patient in the frontal region) and in 1 patient transient circulatory disorders in the brain

	<p>periventricular areas and "beads-shaped" vasoconstrictive changes in the cerebral blood vessels were revealed in angio mode. It was found out that these vasoconstrictive changes persist for 3 months.</p>	<p>in addition, hypotrophy was identified in the cerebral cortex, small focal gliosis in the white matter of the cerebral hemispheres, infiltrative changes in subcortical structures and periventricular areas and "beads-shaped" vasoconstrictive changes in the cerebral blood vessels were revealed. It was found out that these vasoconstrictive changes persist for 3 months.</p>
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In the first group (n = 23) there were no focal signs in the brain in the T1, T2, FLAIR modes, no brain changes were revealed in 21.7% of patients, in 88.9% of patients hypotrophy in the cerebral cortex, small focal gliosis in the white matter of the cerebral hemispheres, infiltrative changes in subcortical structures and periventricular areas were detected (table 1), vasoconstrictive changes in the cerebral blood vessels were revealed in MR angiographic (Figure 3).

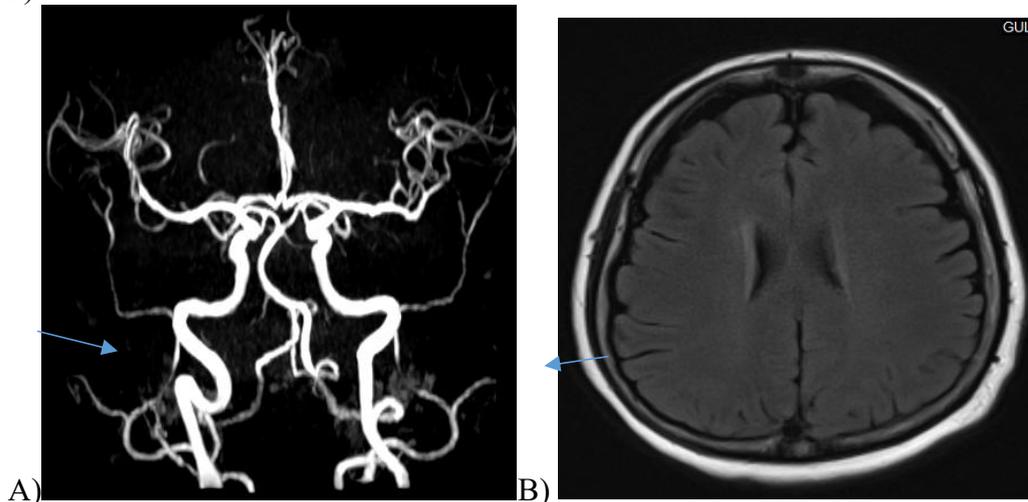


Figure 3. In the patient of the first group MR angiography revealed vasoconstrictive changes in the vessels of medium and small caliber (A), with MRT in T1 mode, expansion of the beds of the brain and lateral ventricles (B) were detected.

USDS examination revealed atherosclerotic changes in cerebral vessels, grade I stenosis in 26% of patients (Fig. 4).

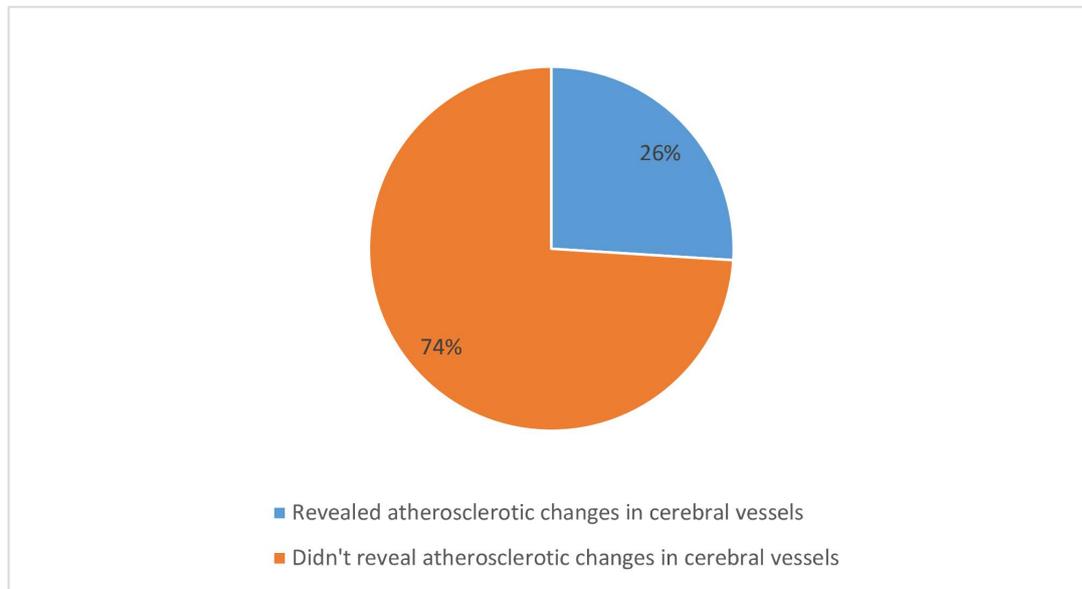
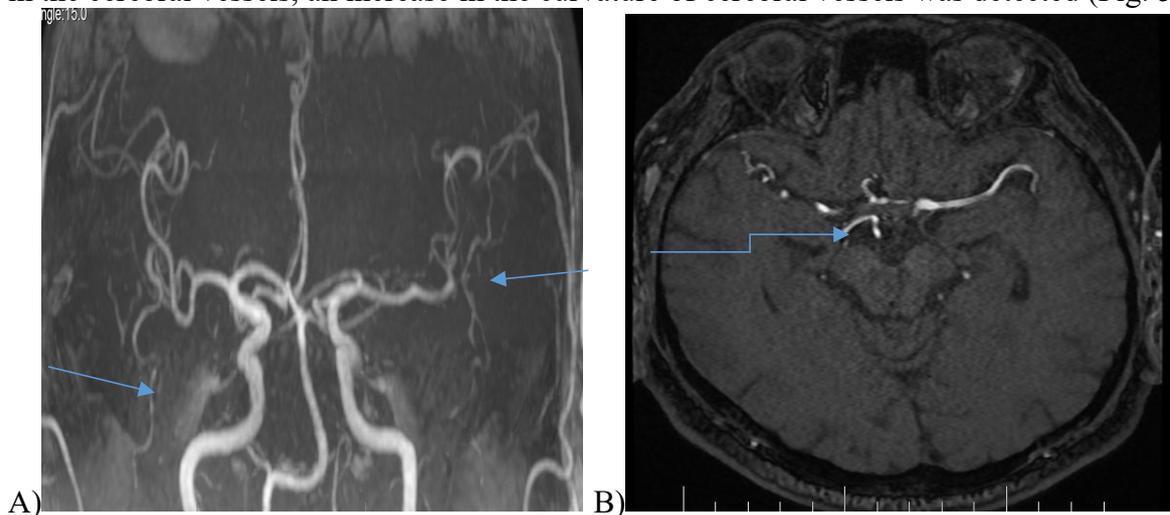


Figure 4. Results of USDS examination in the first group of patients (n = 23).

In the second group in (n=7) 6 patients in T1, T2, FLAIR mode, focal changes in the hemispheres of the brain (in 28.5% of patients in the parietal region of the cerebral hemisphere, in 28.5% of patients in the occipital region, in 14% of patients in the upper frontal region, in 14% of patients in the frontal region) and in 14% patient transient circulatory disorders in the brain were revealed. In addition, hypotrophy was identified in the cerebral cortex, small focal gliosis in the white matter of the cerebral hemispheres, infiltrative changes in subcortical structures and periventricular areas (Table 2).

In MR angiographic examination, along with a sharp manifestation of vasoconstrictive changes in the cerebral vessels, an increase in the curvature of cerebral vessels was detected (Fig. 5).



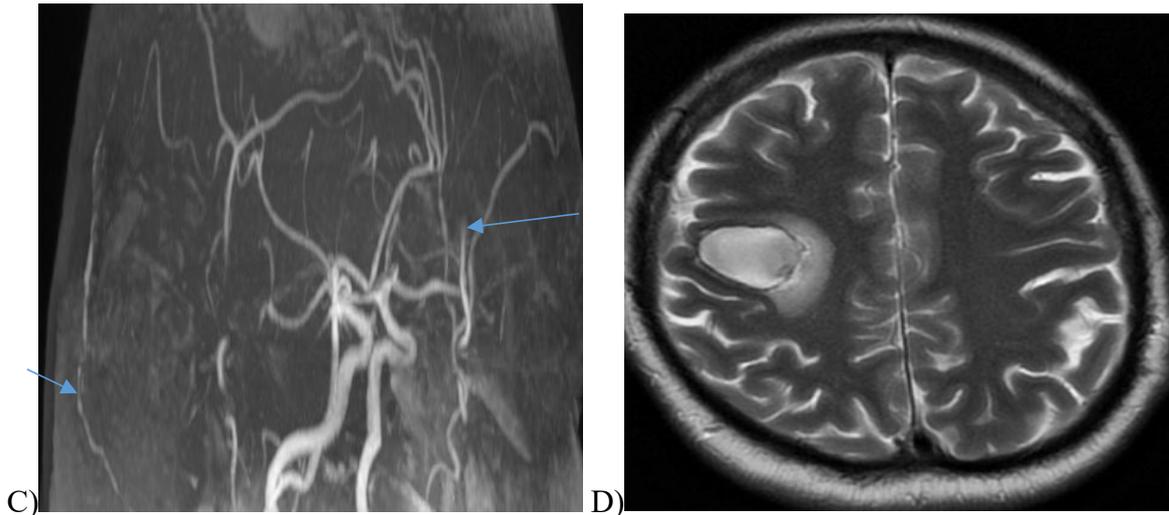


Figure 5. In the patents of the second group vasoconstrictive changes in MR angiography (A, B, C), MRT in T2 mode revealed hematoma and expansion of the beds of the brain (D). USDS examination revealed 42% of atherosclerotic changes in cerebral vessels, grade I or II stenosis (Fig. 6).

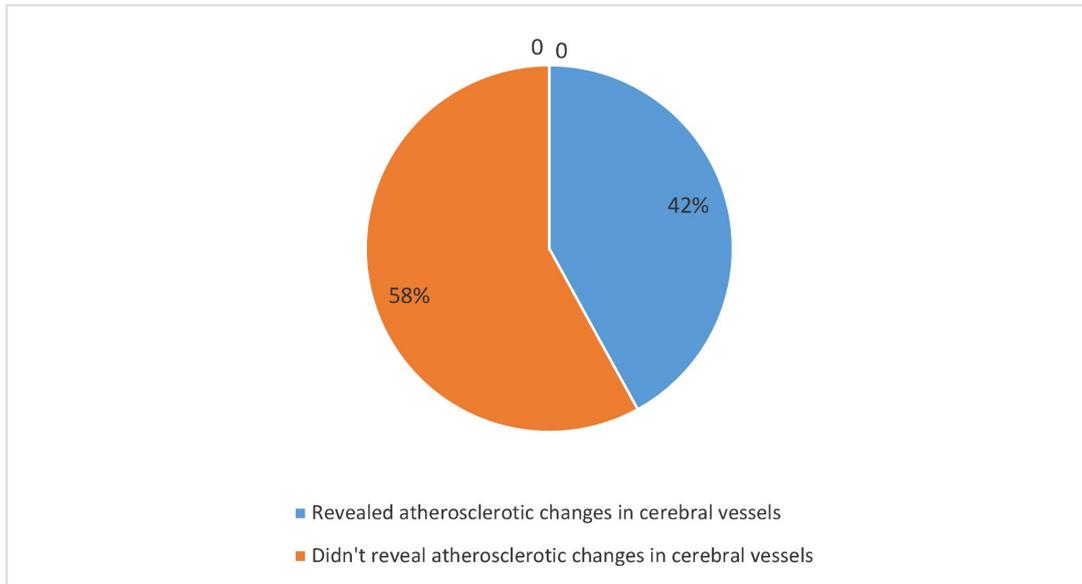


Figure 6. Results of USDS of the cerebral vessels in the second group of patients. Clinical neurological and neuroimaging studies in both groups of patients were especially aimed at determining the state of upper nerve activity and the following results were obtained. When we examined 30 selected patients on the scale VAS: In the first group (n = 23), 30% of patients had severe headaches, 57% had excessively severe headaches, and 13% had unbearable headaches on the VAS scale, slight and moderate-intensity headaches were not observed. In the second group (n = 7), 71% of patients had excessively severe headaches on VAS scale, 19% of patients had unbearable headaches, slight, moderate, severe headaches were not observed. (Table 2).

Table 2. The results of patients with reversible cerebral vasoconstrictive syndrome on the VAS scale.

	The first group (n=23)	The second group (n=7)
0 points normal	not observed	not observed
1-3 points mild headache	not observed	not observed
4-6 points moderate and severe headache	30%	not observed

7-9 points excessively severe headache	57%	71%
10 points unbearable headache	13%	19%

We used the MMSE scale to assess the mental status of the selected 30 patients. In the first group (n = 23), 48% of patients had normal condition, 43% had mild cognitive impairment, and 9% had mild dementia. In the second group (n = 7), 14% had normal condition, 28% had mild cognitive impairment, 44% had mild dementia, 14% of patients could not be examined (due to motor aphasia) (Table 3). In both groups, mild or severe impairment of dementia was not observed.

Table 3. The results of patients with reversible cerebral vasoconstrictive syndrome on MMSE scale.

	The first group (n=23)	The second group (n=7)
28-30 points – normal	48%	14%
24-27 points mild cognitive impairments	43%	28%
20-23 points mild degree dementia	9%	44%
11-19 points moderate degree dementia	not observed	not observed
0-10 points severe degree dementia	not observed	not observed

In addition, we used the Reysberg scale (2008) to assess the decrease in overall cognitive activity in 30 patients.

In the first group (n = 23), 22% of patients had normal memory, 56% had subjective memory impairment, and 22% had mild cognitive impairment. Moderate, severe or excessively severe cognitive impairment was not observed.

In the second group (n = 7), 14% of patients had normal memory, 14% had subjective memory impairment, 43% had mild cognitive impairment, and 14% had moderate cognitive impairment. Severe or excessively severe cognitive impairment was not observed. (Table 4).

Table 4. The results of patients with reversible cerebral vasoconstrictive syndrome on Reysberg scale for assessing total memory (2008).

	The first group	The second group
Norm	22%	14%
Subjective cognitive function is impaired	56%	14%
Cognitive activity is slightly impaired	22%	43%
Cognitive activity is moderately impaired	not observed	14%
Cognitive activity is severely impaired	not observed	not observed
Cognitive activity is extremely severely impaired	not observed	not observed

Nimodipine injection or tablet, Magnesium sulfate are used as the basic treatment for RCVS. The complex treatment included neuroprotection, antioxidants, differential treatment anticoagulant (hemorrhagic stroke), coagulants (ischemic stroke) and symptomatic therapy.

Analysis of the obtained results: Average age of patients with RCVS (Fleming- Call syndrome) is 43.3 years, when evaluating the patient's headache on the VAS scale high-intensity headache is observed, in complicated RCVS, headache is observed at high intensity and of unbearable type. Besides, when examining the patients with RCVS (Fleming-Call syndrome) on Reisberg scale

for assessing total memory (2008), mild cognitive impairments or subjective cognitive impairments in the first group and in the second group dementia of mild degree or mild cognitive impairments were revealed. In addition, in the anamnesis of 82% of patients of both groups migraine was noted. The MRI and MR angiography examination of patients with RCVS revealed the expansion of cerebral ventricles as well as patches of the brain cortex, one-sided or double-sided “beads-shaped” vasoconstrictive changes in the vessels of medium and small caliber. It was established that these vasoconstrictive changes persist for 3 months.

Patients with hemorrhagic stroke caused by RCVS (Fleming-Call syndrome) have severely manifested vasoconstrictive changes in the blood vessels and worm-like curvatures in the cerebral arteries. In addition, relatively benign course of the cerebral stroke caused by this syndrome was determined. Stroke caused by RCVS (Fleming - Call syndrome) is characterized by severe high intensity headache, impaired cognitive function. When making differential diagnosis of RCVS and migraine, moderate and high intensity headache (4-6 points on VAS scale) is observed, MRI and MR angiographic examination do not detect pathological changes in the brain and vasoconstrictive changes in the cerebral vessels [14]. Differential diagnosis of aneurysmal cerebral hemorrhage and hemorrhage caused by RCVS determined vasoconstrictive changes in the cerebral blood vessels, which are close to aneurysm in patients with aneurysmal cerebral hemorrhage; maximal duration of vasospasm is 4 weeks [16], clinical picture, transcranial dopplerography (TCD) and particular radiologic data, i.e. relapsing headache of high intensity is due to the rupture of aneurysm in the intracranial blood vessels [10]. TCD examination shows increased blood flow [3], the cerebral angiography reveals cerebral vasospasm of moving character, vasospasm in one or two cerebral arteries and vasoconstriction reaches peak in 4–11 days [15].

Conclusions: 1. Basically, cerebral stroke caused by RCVS (Fleming-Call syndrome) occurs in patients under the age of 55.

2. Migraine is observed in the anamnesis of patients with cerebral stroke caused by RCVS (Fleming-Call syndrome).

3. Cerebral stroke caused by RCVS (Fleming-Call syndrome) are characterized by specific high-intensity headache, vasoconstrictive changes in cerebral vessels, persistence of the cerebral vasoconstriction for 3 months and mild cognitive impairment.

4. Cerebral stroke caused by RCVS (Fleming-Call syndrome) has a benign course as compared with the cerebral stroke caused for other reasons.

References:

1. Chen Ch, Yu, Chen Sh, P, Fuh J, L, Lirng J,F, Chang F,Ch, Wang Y,F, Wang Sh,J. Vascular wall imaging in reversible cerebral vasoconstriction syndrome – a 3-T contrast-enhanced MRI study // *The Journal of Headache and Pain* – 2018. vol – 19. – P. 74.
2. Chen SP, Fuh JL, Lirng JF et al Recurrence of reversible cerebral vasoconstriction syndrome: a long-term follow-up study. // *Neurology* – 2015. Vol – 84.– P - 1552–1558.
3. Elisabeth B.Marsh, Wendy C. Ziai, Rafael Llinas H. The Need for a Rational approach to vasoconstrictive syndromes: transcranial Doppler and calcium channel blockade in reversible cerebral vasoconstriction syndrome. Case Report // *Neurology* – 2016. Vol 8. - p.161 – 171.
4. John S., Singhal A.B., Calabrese L. et al. Long-term outcomes after reversible cerebral vasoconstriction syndrome // *Cephalalgia*. — 2016. Vol — 36(4). — P. 387-94.
5. Grooters G.S., Sluzewski M., Tijssen C.C. How often is thunderclap headache caused by the reversible cerebral vasoconstriction syndrome? // *Headache*. — 2014. Vol — 54.— P. 732-35.
6. Kim T., Ahn Sh., Sohn C.H. et al. Reversible cerebral vasoconstriction syndrome at the emergency department // *Clin. Exp. Emerg. Med.* — 2015. Vol — 2(4).— P. 203-209.
7. Lee MJ, Cha J, Choi HA et al Blood-brain barrier breakdown in reversible cerebral vasoconstriction syndrome: implications for pathophysiology and diagnosis. *Ann Neurol* – 2017. vol – 81.– p - 454–466.

8. Mehmet A Topcuoglu, Aneesh B.Singhal. Hemorrhagic Reversible Cerebral Vasoconstriction Syndrome feature and mechanism //Stroke - 2016. P.1742-1747.
9. Mehmet A Topcuoglu. Gender and hormonal influences in reversible cerebral vasoconstriction syndrome. //European stroke journal – 2016. vol.I(3). P.199-204.