ISSN: 2181-3906 2026

International scientific journal
«MODERN SCIENCE AND RESEARCH»
VOLUME 5 / ISSUE 4 / UIF:8.2 / MODERNSCIENCE.UZ

CLINICAL-NEUROLOGICAL, NEUROIMAGING, AND DIAGNOSTIC FEATURES OF CALL-FLEMING SYNDROME

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https://doi.org/10.5281/zenodo.19593926

Abstract. *Call-Fleming syndrome, or reversible cerebral vasoconstriction syndrome (RCVS), is a clinico-radiological syndrome characterized by thunderclap headache, segmental or multifocal narrowing of the intracranial arteries, and their regression over time [1–4]. In practice, diagnosis is often delayed because of the polymorphic clinical course of the syndrome, its similarity to other cerebrovascular and headache syndromes, and the fact that early neuroimaging does not always provide clear confirmation [4–6].*

The aim of this study was to evaluate clinical-neurological signs, trigger factors, neuroimaging and paraclinical findings, conformity with diagnostic criteria, and outcomes of clinical management in patients with Call-Fleming syndrome. The study was conducted as a prospective, single-center, observational cohort. Between 2023 and 2025, 30 patients diagnosed with or clinically suspected of having Call-Fleming syndrome were followed in the 1st and 2nd Neurology Departments of the Andijan State Medical Institute Clinic. The results showed that 76.7% of patients were women, and postpartum cases accounted for 30.0%. Thunderclap headache occurred in 96.7% of cases, segmental or multifocal vasoconstriction in 80.0% of patients, and reversibility was documented in 73.3%.

Among trigger factors, vasoactive/serotonergic drugs (40.0%) and postpartum/hormonal factors (30.0%) were predominant. Full conformity with diagnostic criteria was found in 70.0%, partial conformity in 20.0%, and suspected cases accounted for 10.0%. Conservative treatment based on nimodipine predominated, and overall complete clinical regression was recorded in 66.7% of patients [15–18]. These findings indicate that targeted identification of triggers, detection of vasoconstriction using MRA/CTA, and dynamic follow-up are crucial for the early diagnosis of Call-Fleming syndrome.

Keywords: *Call-Fleming syndrome, reversible cerebral vasoconstriction syndrome, thunderclap headache, trigger factors, vasoconstriction, postpartum, reversibility, nimodipine, ICHD-3.*

Introduction

Call-Fleming syndrome is more commonly referred to in the modern literature as reversible cerebral vasoconstriction syndrome (RCVS), and it is a dynamic cerebrovascular syndrome characterized by reversible segmental or multifocal narrowing of the intracranial arteries [1–4]. The core of this syndrome consists of three components: onset with acute and often thunderclap headache, the presence of multifocal vasoconstriction in the cerebral arteries, and regression of these changes usually within 12 weeks [1–4, 11, 14]. In this regard, Call-Fleming syndrome should be viewed not merely as a headache syndrome, but as a complex entity that combines clinical, radiological, and temporal features.

The practical importance of the disease is determined by several factors. First, it often begins with thunderclap headache and requires differential diagnosis with aneurysmal subarachnoid hemorrhage, primary angiitis of the central nervous system (PACNS), venous sinus thrombosis, arterial dissection, migraine, and posterior reversible encephalopathy syndrome (PRES) [4, 10–14]. Second, vasoconstriction may not always be detected on initial neuroimaging, which increases the risk of a false-negative diagnosis [11, 14]. Third, in some cases the syndrome is accompanied by ischemic or hemorrhagic complications, seizures, focal neurological deficits, and alterations in consciousness [7, 8, 10]. Therefore, clinical vigilance, dynamic follow-up, and the sequence of neuroimaging studies are of major practical importance.

In local clinical practice, systematic study of the demographic, clinical-neurological, trigger-related, and neuroimaging characteristics of Call-Fleming syndrome is important, especially for clarifying the diagnostic algorithm in patients presenting with thunderclap headache.

Therefore, the present study was aimed at forming the main clinico-radiological profile of Call-Fleming syndrome in a local cohort.

Study Objective

To evaluate clinical-neurological signs, trigger factors, neuroimaging and paraclinical findings, conformity with diagnostic criteria, as well as treatment and clinical management outcomes in patients with Call-Fleming syndrome.

Materials and Methods

This study was organized as a prospective, single-center, observational cohort design. The study was conducted during 2023–2025 at the 1st and 2nd Neurology Departments of the Andijan State Medical Institute Clinic. Thirty consecutive patients diagnosed with or clinically suspected of having Call-Fleming syndrome were included. Clinical records, history, neurological status, triggers, paraclinical data, and neuroimaging findings were analyzed systematically.

Clinical-anamnestic assessment included the onset pattern of thunderclap headache, time to maximal intensity, recurrence pattern, possible triggers, age, sex, and reproductive status.

Neurological evaluation included focal deficits, seizures, autonomic disturbances, general cerebral symptoms, state of consciousness, and cognitive complaints. The clinical course was systematized into three main phenotypes: headache-dominant form, focal-neurological form, and complicated/severe form.

Neuroimaging investigations included MRI/MRA, CT/CTA, and, when necessary, MRV, transcranial Doppler, and perfusion assessment. Lumbar puncture was performed in patients who required additional differential diagnosis. Diagnostic conformity was assessed according to current clinical and radiological criteria for Call-Fleming syndrome as “fully consistent,” “partially consistent,” and “suspected”; the RCVS2 scoring system was used as an auxiliary tool [9, 12, 13]. Statistically, the results were summarized mainly in descriptive form; $p<0.05$ was accepted as the threshold of statistical significance, and calculations were performed using SPSS.

Results

Of the 30 patients included in the study, 23 were women (76.7%) and 7 were men (23.3%).

Among the women, 9 patients were in the postpartum period, which accounted for 30.0% of the entire cohort. The mean age was 38.6±9.4 years, the median age was 37 (31–45) years, and the age range was 22–58 years.

By age group, patients aged 30–39 years constituted the largest proportion, with 11 patients (36.7%). The 40–49 year age group included 8 patients (26.7%), the 20–29 year age group 6 patients (20.0%), and the 50–59 year age group 5 patients (16.6%).

Thunderclap headache was the leading clinical signal in the cohort. It was recorded in 29 patients (96.7%), and recurrent thunderclap attacks were observed in 27 patients (90.0%). Nausea or vomiting occurred in 15 patients (50.0%), photophobia or autonomic disturbance in 12 patients (40.0%), focal neurological deficit in 7 patients (23.3%), seizures in 4 patients (13.3%), confusion in 5 patients (16.6%), and cognitive complaints in 3 patients (10.0%). In clinical phenotyping, the headache-dominant form was found in 18 patients (60.0%), the focal-neurological form in 7 patients (23.3%), and the complicated/severe form in 5 patients (16.7%).

Among trigger factors, vasoactive or serotonergic drugs accounted for the largest share and were noted in 12 patients (40.0%). Postpartum/hormonal factors were identified in 9 patients (30.0%), emotional stress and physical exertion each in 5 cases (16.7%), and Valsalva- or sexual activity-related triggers in 4 cases (13.3%). In 6 patients (20.0%), several triggers were present simultaneously. Comparative trigger–phenotype analysis showed that postpartum/hormonal factors were more often associated with the headache-dominant form, while vasoactive/serotonergic drugs appeared to be related to more complicated or focal-neurological forms.

Neuroimaging revealed segmental or multifocal vasoconstriction in 24 patients (80.0%), which was the main radiological sign. In addition, 1 patient had PRES-type changes, 1 patient had convexity subarachnoid hemorrhage, and 2 patients had infarction or ischemic lesions. In 3 cases, neuroimaging findings were absent or remained inconclusive. Reversibility was documented in 22 patients (73.3%). Lumbar puncture was performed in 6 patients, and cerebrospinal fluid was normal or near normal in 5 of them.

Diagnostic assessment showed that 21 patients (70.0%) were fully consistent with the diagnosis, 6 patients (20.0%) were partially consistent, and 3 patients (10.0%) were categorized as suspected cases. According to the RCVS2 scoring system, 19 patients had a score of 5 or higher, 6 patients scored 3–4, and 5 patients scored 2 or lower. In 3 cases from the low-score group, RCVS was later excluded. In treatment, nimodipine was used in 26 patients (86.7%); verapamil or nicardipine in 4 patients (13.3%), magnesium sulfate in 3 postpartum cases (10.0%), intra-arterial vasodilators in 4 patients (13.3%), and milrinone in 1 patient (3.3%). Regarding outcomes, complete regression was observed in 20 patients (66.7%), partial improvement in 7 patients (23.3%), and persistent deficit or complication in 3 patients (10.0%).

Discussion

The obtained results showed that Call-Fleming syndrome occurred predominantly in women, especially those of reproductive age and in the postpartum period. This demographic pattern is consistent with the view that the syndrome is sensitive to hormonal and autonomic factors [2, 6–8]. The occurrence of thunderclap headache in 96.7% of cases and recurrent attacks in 90.0% of patients confirmed that thunderclap headache is the main clinical core of this syndrome [1–4, 8]. The polymorphic nature of the clinical phenotypes showed that it is insufficient in practice to assess Call-Fleming syndrome merely as a “headache-only” syndrome; cases with focal deficit, seizures, and altered consciousness corresponded more often to

complicated neuroimaging findings, suggesting a certain relationship between clinical severity and radiological severity in this syndrome [7, 8].

The predominance of vasoactive/serotonergic drugs and postpartum/hormonal conditions among trigger factors justifies actively searching for these factors during history-taking [5–8].

This is especially important in patients presenting with thunderclap headache and inconclusive initial investigations. The identification of vasoconstriction in 80.0% of patients and documented reversibility in 73.3% indicate the superiority of dynamic imaging in the diagnosis of Call-Fleming syndrome [11, 14, 19–21]. Because initial imaging may be negative or equivocal, repeated MRA/CTA is important when clinical suspicion remains high. The mostly normal lumbar puncture results also served as additional evidence in the differential diagnosis, helping to exclude inflammatory vasculitides and aneurysmal hemorrhagic conditions [10–14].

The presence of partially consistent and suspected cases in the diagnostic assessment showed that it is insufficient to rely on only one clinical criterion or one radiological finding when diagnosing Call-Fleming syndrome. An integrated evaluation of ICHD-3 criteria, triggers, vascular imaging, cerebrospinal fluid findings, and dynamic follow-up is the most appropriate approach [9, 10–14]. Treatment outcomes demonstrated the practical advantage of nimodipine-based conservative management, although this should be interpreted together with the patients' baseline clinical severity [15–18]. Although intensified or endovascular strategies were used in severe and complicated patients, their outcomes may have been related to the initial risk profile [16–18].

Conclusion

In the local cohort, Call-Fleming syndrome occurred predominantly in women, especially patients of reproductive age and in the postpartum period. The clinical core of the syndrome was represented by thunderclap headache and its recurrent attacks, while trigger factors were mainly vasoactive/serotonergic drugs and postpartum/hormonal conditions. Neuroimaging showed that segmental or multifocal vasoconstriction was the principal sign, and reversibility was confirmed in most cases. Diagnostic evaluation indicated the need for integrated assessment of clinical, trigger-related, neuroimaging, and dynamic data in order to confirm Call-Fleming syndrome.

Nimodipine-based conservative management produced favorable results in most patients.

These findings provide a practical basis for early recognition of Call-Fleming syndrome, optimization of differential diagnosis, and improvement of clinical management in patients presenting with thunderclap headache.

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