Цереброкардіальний синдром при ішемічному інсульті

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Цереброкардіальний синдром розглядається як комплекс серцевих порушень, які виникають на фоні ураження центральної нервової системи та найчастіше розвиваються внаслідок церебрального інсульту. Подано опис клінічного випадку цереброкардіального синдрому у хворого з ішемічним інсультом, результати діагностичних заходів, динаміка електрокардіограми. Клінічне значення цереброкардіального синдрому полягає в тому, що він може викликати діагностичні помилки та гіпердіагностику серцевої патології в ситуаціях, коли її немає, і, відповідно, призвести до неправильного лікування. Індивідуальний підхід до оцінки серцевих розладів у пацієнтів з церебральним інсультом і знання закономірностей змін нейроендокринної, імунної систем, системи гемостазу забезпечать своєчасну діагностику цереброкардіального синдрому, оптимізацію лікування і поліпшать прогноз.

Ключові слова: цереброкардіальний синдром, церебральний інсульт, ішемічний інсульт, серцеві аритмії.

OPEN ACCESS

DOI 10.25040/ntsh2022.01.09

Адреса для листування: Військово-медичний клінічний центр Західного регіону, м. Львів, вул. Личаківська,26, Україна, 79010

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Надійшла до редакції: 10.04.2021
Прийнята до друку: 19.01.2022
Опублікована онлайн: 27.06.2022

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Конфлікт інтересів: автори декларують відсутність конфлікту інтересів.

Особистий внесок авторів
Концепція: Сергій Стаднік;
Результати досліджень: Сергій Стаднік;
Написання статті: Сергій Стаднік;
Редагування та затвердження остаточного варіанта: Сергій Стаднік.

Дозвіл комісії з біоетики щодо проведення досліджень: не потрібний. Письмову поінформовану згоду було отримано від пацієнта, який брав участь у дослідженні.

Фінансування: автори декларують відсутність фінансування.

Cerebrocardial syndrome in ischemic stroke

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Cerebrocardial syndrome is a complex of cardiac disorders that occur against the background of damage to the central nervous system and most often develop as a result of cerebral stroke. The article presents a description of a clinical case of cerebrocardial syndrome in a patient with ischemic stroke, the results of diagnostic measures, the dynamics of the electrocardiogram. The clinical significance of cerebrocardial syndrome is that it can cause diagnostic errors and overdiagnosis of cardiac pathology in situations where it does not exist, and, accordingly, lead to improper treatment. An individual approach to the assessment of cardiac disorders in patients with cerebral stroke and regular changes in the neuroendocrine, immune systems, hemostasis system will provide for a timely diagnosis of cerebrocardial syndrome, optimization of treatment and improved prognosis.

***Keywords*:** Cerebrocardial syndrome, cerebral stroke, ischemic stroke, cardiac arrhythmias.

OPEN ACCESS

DOI 10.25040/ntsh2022.01.09

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Received: Apr, 4, 2021

Accepted: Jan, 19, 2022

Published online: June, 27, 2022

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Disclosures: the authors declared no conflict of interest.

Author Contributions
Conceptualization: Sergiy Stadnik;
Results of study: Sergiy Stadnik;
Writing: Sergiy Stadnik;
Review & editing: Sergiy Stadnik.

Ethical approval: Not required.
Written informed consent was obtained from the patient who participated in the study.

Funding: the authors declared no funding.

Cerebral strokes constitute a problem of medical and social importance, as they pose a threat to life and health around the world. Ischemic stroke, one of their types, has a leading role, which is associated with its high prevalence, disability, and mortality. A wide range of modifying risk factors for stroke (arterial hypertension, diabetes, obesity, atrial fibrillation) with the insufficient correction or lack thereof, significantly worsen the course of stroke and adversely affect its prognosis. The greatest risk associated with the risk of death is represented by cardiac disorders that develop or worsen in patients with cerebral stroke, as they may result in neurogenic cardiac dysfunction – cerebrocardial syndrome (synonyms: syndrome of acute dysautonomy, diencephalic-catabolic syndrome, sympathetic «storm», neurogenic stress cardiomyopathy) [1, 2, 3].

The damage to the central nervous system leads to transient disorders of the cardiovascular system and more significant changes in the heart. The complex of cardiac disorders caused by acute brain damage is referred to as «cerebrocardial syndrome». This term was proposed in the mid-'50s of the last century to denote certain changes in the electrocardiogram (ECG) associated with brain damage. According to some studies, cerebrocardial syndrome occurs in 15-51% of patients with ischemic stroke [4, 5].

In some cases, manifestations of cerebrocardial syndrome may reflect the existing but previously hidden cardiac pathology. Due to disorders of systemic and cerebral hemodynamics, cardiac disorders can increase ischemic brain damage and worsen the patient's prognosis. The appearance of these changes on the ECG of patients with a stroke and without primary heart disease can complicate the diagnosis and treatment. Therefore, doctors of different specialties (neurologists, cardiologists, therapists, resuscitators) need to know about manifestations of cerebrocardial syndrome, and their timely diagnosis will adjust the treatment of patients with strokes [1, 6].

Toxic, damaging effects of adrenaline and noradrenaline on cardiomyocytes play an important role in the mechanisms of cerebrocardial syndrome development. Cardiac function is regulated by the central nervous system, autonomic nervous system, endocrine and humoral factors. In addition, the heart rate depends on the state of conduction system components. In the development of cerebrocardial syndrome, more focus is placed on the disorder of autonomic regulation with activation of the sympathetic link and increased production of adrenal hormones, which causes increased release of catecholamines into the blood plasma and leads to changes in the morphofunctional properties of cardiomyocytes. Due to the increased activation of the sympathetic nervous system during ischemic stroke, the formation of catecholamines in the presynaptic terminals of nerve fibers increases. In addition, the amount of catecholamines in the systemic circulation increases [1]. High levels of catecholamines were observed for about 3 days with a gradual decrease up to 40 days. A relationship has been established between plasma catecholamine levels and the severity of electrocardiogram changes. The local toxic effect of catecholamines has more significance in the development of cerebrocardial syndrome as compared to their systemic effect [7]. Excessive amounts of catecholamines cause changes in β-adrenoceptors of cardiomyocytes, decreased myocardial contractility. Hypercatecholaminemia causes secondary myocardial damage, which is manifested by the lysis of cardiomyocytes and the development of necrosis foci (so-called «adrenaline myocarditis») [8]. Catecholamines increase the entry of calcium ions into the cell and the release of potassium, which shortens the action potential of cardiomyocytes, which in turn increases the heart rate and can provoke arrhythmias. Calcium ions increase the activity of phospholipase inside the cell, which causes membrane damage and the formation of fatty acids. Excessive amounts of arachidonic acid contribute to the increased generation of free radicals. In addition, it can be converted into prostaglandins, leukotrienes and thromboxanes, which further damage cells. Free radicals, prostaglandins and thromboxane cause vasospasm, increase the aggregation capacity of platelets, thereby contributing to impaired microcirculation. The damage to intracellular membranes causes dysfunction of ribosomes and decreased protein synthesis, which further disrupts metabolism in the cell and reduces the cell resistance to damaging factors. In patients with coronary heart disease, this can cause myocardial infarction, whereas in patients without coronary atherosclerosis, cardiac dysfunction is potentially reversible. An important role in changing the adrenergic structures and

membranes of cardiomyocytes is played by lipid peroxidation, which is activated under stress, which can provoke cardiac arrhythmias [9]. As a result of cell damage in the blood, myocardial enzymes may increase.

Due to the difference in the location of the centers of autonomic regulation in the brain, stroke location may have its own effect on the rate of cardiac disorders. It's noted that supraventricular tachyarrhythmias are more often registered in the right hemispheric localization of stroke, and ventricular tachyarrhythmias are more often registered in the left hemisphere. Right-sided autonomic stimulation has a greater effect on the sinus node, so stimulation or suppression of the right half of the medulla oblongata and hypothalamus has a greater effect on supraventricular ectopic activity. The crust of the islet lobe plays an important role in the regulation of vegetative functions. The damage to different parts of this frontal lobe in different variants of electrocardiographic and clinical manifestations of cerebrocardial syndrome [3].

Cardiac arrhythmias in conditions of impaired autoregulation of cerebral blood flow adversely affect the reparative processes in the area of cerebral ischemia. Even a moderate transient cardiogenic decrease in blood pressure further impairs the blood supply to the periinfarction site. Frequent supraventricular extrasystole can cause a decrease in cerebral blood flow by 7%, ventricular extrasystole – by 12%, ventricular paroxysmal tachycardia – by 40–75%. Prolonged supraventricular paroxysmal tachycardia causes a significant decrease in left ventricular stroke volume with subsequent deterioration of cerebral hemodynamics [10]. According to another theory, hypomagnesemia plays a significant role in the pathogenesis of cerebrocardial syndrome [11].

Cerebrocardial syndrome is characterized by changes in the T-wave, which are characterized by an increase in its duration (increase in the base) and amplitude (height), inversion (negative T-wave). In addition, there may be an increase in the U-wave, spike or depression of the ST segment, creating a picture of a «pseudoinfarction» curve. In contrast to infarct, T-waves in cerebrocardial syndrome are asymmetric, larger in amplitude, wide and dynamic. The reverse dynamics of the final part of the ventricular complex does not reflect positive dynamics of brain damage [12].

In recent years, the concept of cerebrocardial syndrome started including not only changes in the electrocardiogram of the end of the ventricular complex, but also other heart disorders that develop in cerebral lesions: cardiac arrhythmias, QT prolongation, cardiac arrhythmias, systolic and diastolic left myocardial dysfunction ventricle. The most common arrhythmias are: sinus bradycardia (rarely tachycardia), sinus node arrest, atrioventricular block, ventricular or atrial extrasystole, atrial fibrillation, slow atrioventricular rhythm. Sometimes there is a violation of intraventricular conduction in the form of transient blockades of one of the legs of the bundle of His [13]. The cerebrocardial syndrome is characterized by rapid reverse dynamics, which does not reflect the direction of the cerebral process.

The most common arrhythmia in the acute period of cerebral circulatory disorders is atrial fibrillation, which is associated with a high incidence of cardioembolism and significantly increases the frequency of recurrent strokes [10]. In addition, in cardioembolic stroke compared with atherothrombotic and hemodynamic ones, atrial fibrillation, ventricular extrasystoles and blockade of the legs of the bundle of His are significantly more common [14]. This type of stroke is characterized by a more severe course and slower recovery of neurological deficit. The relationship between the location of the lesion associated with a particular vascular basin and changes in the electrocardiogram: atrial fibrillation and tachycardia are more common if the lesion is localized in the left middle cerebral artery, and bradycardia and atrial conduction disorders – when it is localized in vertebrobasilar basin [3].

In other studies, patients with an anamnesis of acute stroke without a history of cardiac pathology increased supraventricular and ventricular ectopic activity, which is probably due to cerebrogenic effects. In the most acute phase of ischemic stroke, an increase in supraventricular and ventricular ectopic activity and changes in heart rate, which depended on the size and location of the ischemic focus, were registered. After the acute period of stroke, cerebrocardial syndrome regressed in most patients. Regression of neurological deficit in

the acute phase of ischemic stroke was inversely correlated with the frequency of episodes of bradyarrhythmia [3, 11, 12].

Clinical observations have shown that cardiac injuries can develop immediately or within a few hours after an acute cerebral catastrophe. In hemorrhagic transformation ischemic stroke, which complicates the course of stroke in the acute period, the number of patients with cardiac arrhythmias, namely atrial fibrillation, was significantly larger [3, 13].

Often, a manifestation of cerebrocardial syndrome is the development of systolic dysfunction with hypokinetic changes in the walls of heart according to echocardiography. No less important is the development of diastolic dysfunction with increasing end-diastolic pressure in the left ventricle and activation of the sympathetic nervous system, which causes endothelial dysfunction and the development of hypercoagulation [15].

The diagnosis of cerebrocardial syndrome is quite difficult. Specialists of the Mayo Clinic have proposed four criteria for its diagnosis [16]:
1) impaired motor activity of the left ventricular wall, beyond the blood supply of one artery;
2) no obstruction of the corresponding coronary artery;
3) changes in the electrocardiogram (transient rise of the ST segment or diffuse changes in the T-wave), accompanied by a slight increase in troponin levels;
4) the absence of proven pheochromocytoma or myocarditis.

However, to date, there are no clear guidelines for identifying a risk group for sudden death in patients who have undergone cerebral stroke with cerebrocardial syndrome.

It should be noted that changes occurring in cerebrocardial syndrome regress much faster than neurological deficit and do not correlate with the overall severity of the patient's condition [17]. The biochemical analysis of blood is characterized by an increase in cardio specific creatine phosphokinase. However, its dynamics is significantly different from that of myocardial infarction: the concentration of this enzyme does not regress immediately after the cerebral stroke, and gradually increases over the next four days [18].

Particular attention should be paid to increasing the QT interval in patients with stroke, as this is an adverse factor that provokes arrhythmogenic complications. A QT interval greater than 450 ms is considered an important predictor of such complications and is associated with a threefold risk of sudden cardiovascular death [3].

ECG criteria for assessing the severity of brain pathology were determined: mild – duration of ECG changes 1–2 days (ECG changes are absent or manifested by moderate sinus tachy- or bradycardia, single extrasystoles, moderate depression of the T-wave or ST-segment); moderate – duration up to 6–7 days (clear signs of myocardial ischemia in certain areas: negative T wave, depression or elevation of the ST segment more than 1 mm; there are short-term paroxysms of atrial fibrillation or tachycardia); severe – the duration of 15–20 days or more (frequent extrasystole, paroxysmal tachycardia and atrial fibrillation, ventricular fibrillation, combined arrhythmias, signs of myocardial infarction) [19].

The clinical significance of cerebrocardial syndrome is that it can cause diagnostic errors and overdiagnosis of cardiac pathology in situations where it does not exist, and, accordingly, lead to improper treatment.

Clinical case of cerebrocardial syndrome at an ischemic stroke from the author's archive:

Patient D., 57 years old, was admitted to the angio-neurological department with complaints of visual disturbances in the form of his loss when looking to the left, speech disorders, dizziness, shakiness when walking.

According to the patient, the condition and state of health suddenly deteriorated the day before, when there were visual disturbances when looking to the left, dizziness, shakiness when walking. The next day he came to the hospital and was hospitalized urgently.

For a long time, he suffered from arterial hypertension, type II diabetes, gout. In 2012, he suffered an ischemic stroke in the left middle cerebral artery.

Neurological status: stroke severity on the NIHSS scale – 10 points, consciousness is preserved – 15 points on the Glasgow scale. Iso-

corrhea, nystagmus, diplopia were not detected. Homonymous hemianopsia on the left. Dysarthric language. Right hemiparesis, hemihypesthesia. Deep reflexes D> S. Pathological foot like Babinsky's case. There are no meningeal signs.

Preliminary diagnosis: Cerebrovascular disease. Atherothrombotic ischemic stroke in the basin of the right posterior cerebral artery in the form of left homonymous hemianopsia, dysarthria. Consequences of ischemic stroke (2012) in the basin of the left middle cerebral artery in the form of right hemiparesis, hemihypesthesia. Chronic cerebral ischemia stage III.

Clinical and biochemical blood tests – without abnormalities. ECG on admission (fig. 1): sinus rhythm, irregular, heart rate – 75/min., ventricular extrasystoles, increase in the amplitude of a tooth of T in assignment V_2, inversion of a T-wave in assignments I, II, aVL, V_5-V_6, signs of hypertrophy of the left ventricle are registered.

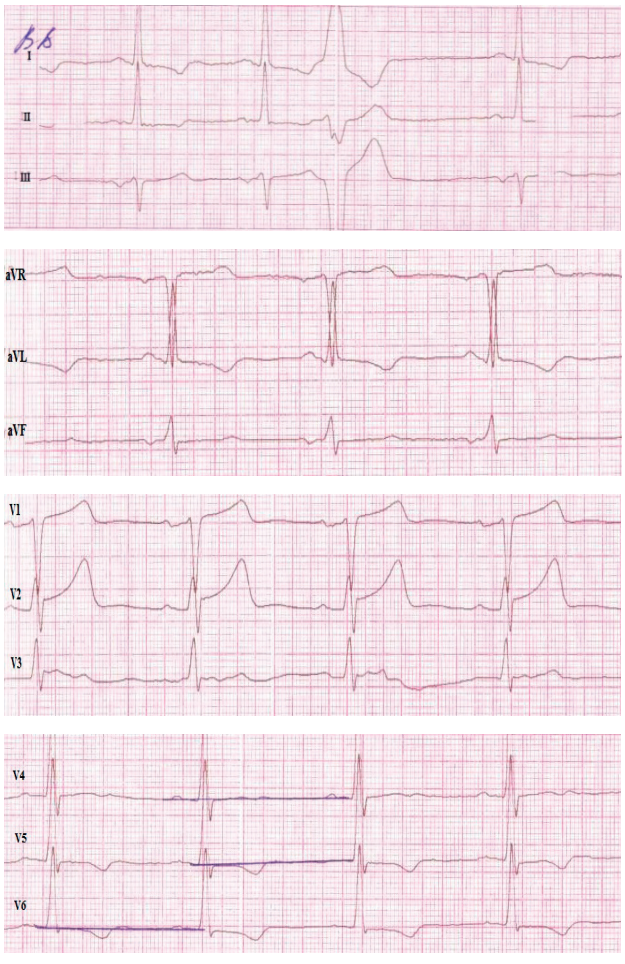

Fig. 1. ECG of the patient D. at receipt

ECG in the dynamics (after 3 days) (fig. 2): sinus rhythm, regular, heart rate – 64/min., extrasystoles are not registered, normalized segment S-T and T-wave in the chest leads.

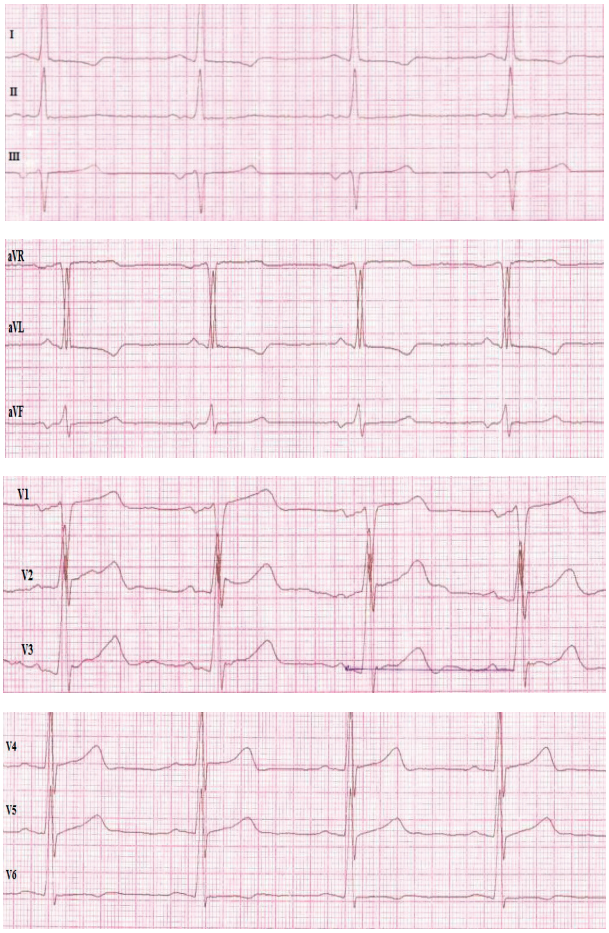

Fig. 2. Dynamics of an ECG of the patient D. in 3 days

In computed tomography of the brain (fig. 3), hypertensive zones with clear contours with a density of +3+12 units are visualized in the left hemisphere of the cerebellum. H (fig. 3A); in the right hemisphere of the brain, the extensive ischemic site with a density of +15+24 units is traced. (fig. 3B). The ventricular system is expanded: III ventricle up to 1.7 cm wide, lateral ventricles up to 2.4 cm wide (fig. 3C). Middle structures are not displaced. Convex spaces, furrows, fissures are expanded in both hemispheres of the brain, local ischemic areas are traced. Conclusion: CT signs of cerebrovascular disorders of the ischemic type in the right hemisphere of the brain, cerebrospinal fluid cysts of the left hemisphere of the cerebellum.

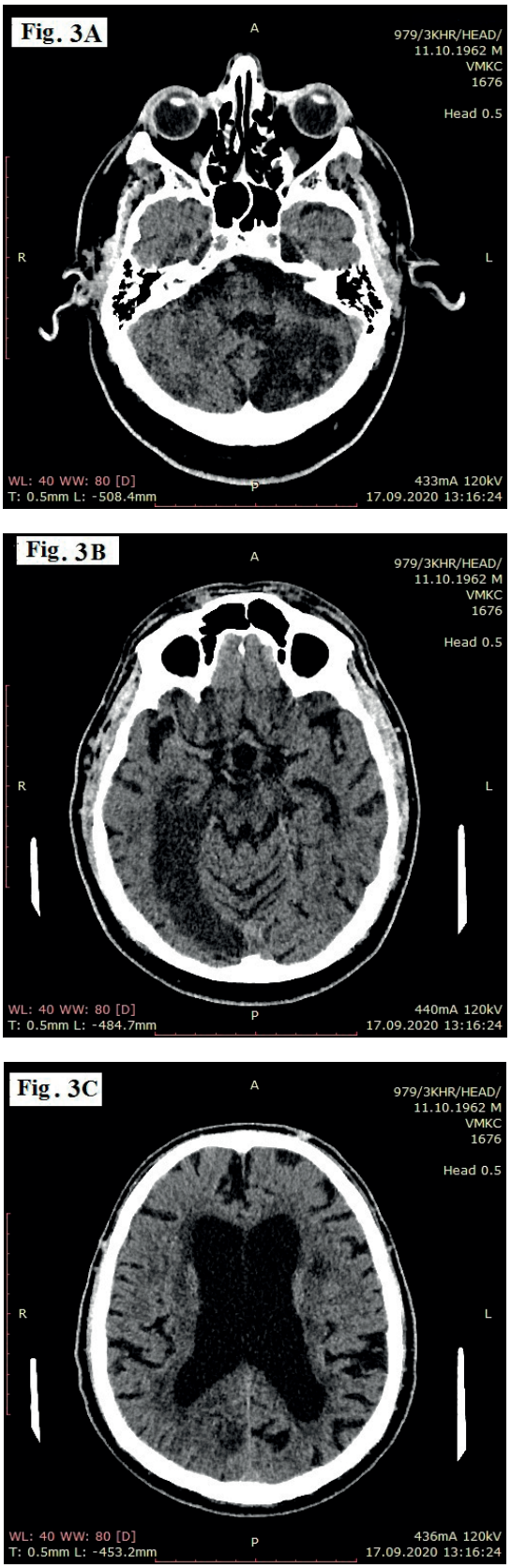

Fig. 3. CT of patient D

The patient received traditional therapy for the stroke (acetylsalicylic acid, low molecular weight heparin, antihypertensive drugs, β-blockers, statins, intravenous infusion therapy and neuroprotective agents).

The described case demonstrates typical manifestations of cerebrocardial syndrome when infarct-like ECG changes were not a manifestation of heart damage, but a reflection of the involvement of cerebral structures. To sum up, cardiac disorders in ischemic stroke are an understudied field of cardioneurology. Ischemic stroke is associated with an increased incidence of cardiac arrhythmias, which, under conditions of disruption of cerebral blood flow autoregulation, even with basic optimality of central hemodynamics, can worsen cerebral perfusion and interfere during the early rehabilitation period.

Cardiac disorders in stroke are diverse, ranging from electrocardiographic phenomena involving changes in the terminal part of the ventricular complex to severe arrhythmias. Clinical and electrocardiographic manifestations of cerebrocardial syndrome, as well as their duration in stroke, depend on the localization of the focus and the extent of brain damage. It is not excluded that the latent cardiac pathology that existed before the stroke on the manifestations of cerebrocardial syndrome is not excluded.

An individual approach to the assessment of cardiac disorders in patients with cerebral stroke and knowledge of the regular changes in the neuroendocrine, immune systems, hemostasis system will provide a timely diagnosis of cerebrocardial syndrome, optimization of treatment and improved prognosis.

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