Archives of Neurology and Neuro Disorders

Volume 1, Issue 1, 2018, PP: 21-24

Stroke Associated with Reduced Protein S in Young Adult Brain: A Case Report

Marcelo José da Silva de Magalhães[*1], Janniny Fernanda Lopes Mendes Figueiredo[2] Kelly Viviane Gomes Marques[2], Liliane de Oliveira Melo[2], Luciano Neto Loureiro Freitas[2] Moisés Figueiredo Camargos[2], Henrique Nunes Pereira Oliva[3]

[1*]Professor, Faculdades Unidas do Norte de Minas (FUNORTE), Faculdades Integradas Pitágoras de Montes Claros (FIP-Moc); Neurosurgeon, Hospital Aroldo Tourinho, Montes Claros, MG, Brazil.

[2]Medical student, FUNORTE Montes Claros-MG, Brasil.

[3]Master of Science in Engineering; Medical student, Faculdades Integradas Pitágoras de Montes Claros (FIP-Moc), Montes Claros, MG, Brazil.

marcelo7779@yahoo.com.br

***Corresponding Author:** Marcelo José da Silva de Magalhães, Professor, Faculdades Unidas do Norte de Minas (FUNORTE), Faculdades Integradas Pitágoras de Montes Claros (FIP-Moc); Neurosurgeon, Hospital Aroldo Tourinho, Montes Claros, MG, Brazil.*

Abstract

Stroke is a neurological deficit caused by a brain injury secondary to a vascular mechanism. It can be classified as: ischemic or hemorrhagic. Ischemic form is more common, resulting from insufficient cerebral blood supply. Most patients who suffer strokes have associated diseases such as diabetes, hypertension, dyslipidemia or cardiovascular disease. In the absence of these comorbidities, however, especially in patients younger than 45 years, it should be checked for possible deficiencies of natural anticoagulants such as protein C and protein S. Stroke associated with protein S deficiency is rare, although it is more common in young adults. This clinical report, in turn, aims to describe a case of ischemic stroke associated with reduced protein S in a young patient.

Keywords: *Stroke; Young patients; Protein S deficiency.*

Introduction

Stroke is a pathology that affects the vessels of the brain - a subdivision of the Central Nervous System which comprises the brain, cerebellum and brainstem. [1] It is characterized in a sudden and non-convulsive focal neurological deficit, determined by a cerebral injury, secondary to a vascular and non-traumatic mechanism. [2] It can be classified as ischemic or hemorrhagic due to different etiologies. Hemorrhagic stroke comprises subarachnoid hemorrhage, usually due to the rupture of congenital saccular aneurysms located in the arteries of the Willis polygon and intraparenchymal hemorrhage, whose basic causal mechanism is the hyaline degeneration of cerebral intraparenchymal arteries, with the main disease associated with systemic arterial hypertension. Ischemic stroke describes the neurological deficit resulting from the insufficiency of cerebral blood supply, and may be temporary or permanent, having as main risk factors systemic arterial hypertension, heart diseases and diabetes mellitus. [3]

Stroke disease is one of the biggest causes of mortality and morbidity worldwide. Considered the third most common cause of death in developing countries, besides being the greatest cause of disability among adults. [4] The incidence of stroke increases with aging and doubles with each decade of life from 55 years of age. [5]

However, stroke may occur earlier and be associated to other risk factors, such as coagulation disorders, inflammatory and immune diseases, as well as drug use. Previous studies have shown an incidence of 10% in patients under 55 years of age and 3.9% in patients younger than 45 years of age, showing a minimal incidence in young patients. [6]

Coagulation disorders, in turn, have been described in recent years as a cause of stroke, especially in patients under 40 years of age. They are mainly characterized by deficiency of Proteins S and C, natural anticoagulants. There is a current trend, therefore, to investigate these deficiencies in all young patients with stroke of indeterminate cause and in those with thrombolytic manifestations of multiple systems. [7]

Thus, this clinical report aims to describe a rare case of ischemic stroke, related to the reduction of Protein S in a young patient (43 years).

Case Report

JRCF, 43 years old, male, previously healthy, with no history of arterial hypertension, admitted to the neurology service of Aroldo Tourinho Hospital in Montes Claros, Minas Gerais State, Brazil complaining of right hemiparesis and aphasia for five days. He denied smoking, previous history of familial thrombotic diseases, sickle cell anemia, and cases of familial ischemic stroke. The neurological examination revealed a well-oriented patient in time and space, with right hemiplegia, Broca's aphasia, right hyposthesia and right central facial paralysis. Computed tomography of the skull revealed left anterior Choroidal artery infarction (Figure 1). Laboratory tests of biochemistry yielded the following results: cholesterol 157 mg/dl, triglycerides 115 mg/dl, fasting blood sugar levels of 84 mg/dl, urea 23 mg/dl, creatinine 1.36mg/dl, hemoglobin 15g/dl, total protein 7.3 g/dl, albumin 3.6 g/dl, globulin 3.7 g/dl, Glutamic oxaloacetic transaminase (GOT) 61 U/L, Glutamic pyruvic transaminase (GPT) 30 U/L, GT 59 U/L range, 1.0 U RNI and Functional Protein S 33% (reference value greater than 73%). The inflammatory and immune tests were C-reactive protein (CRP) ≤ 6 mg/dl, Antistreptolysin O (ASO) and non-reactive antinuclear antibody (ANA). The electrocardiogram showed sinus rhythm, regular and without Atrial Fibrillation (AF). The ecodoppler of the carotid and cervical arteries showed no alterations. Given the socioeconomic characteristics of the patient and the difficulty to perform a proper INR control in case of full anticoagulation with Warfarin, it was opted for treatment with antiaggregant only – 325mg Acetylsalicylic Acid / day. After receiving counseling, the patient agreed with the therapeutic option. After 6 months of the ischemic event, the patient presented a mild improvement in right hemiparesis, maintaining Broca's aphasia.

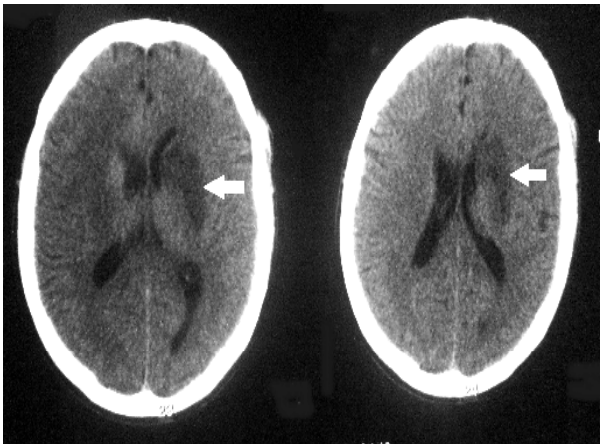

Fig 1. *Computed tomography of the skull without contrast revealing hypodensity compatible with recent ischemic process in territory of the left choroidal artery.*

Discussion

The association between the deficiency of natural anticoagulants (antithrombin III, protein C or S) and ischemic stroke is controversial. Recent reports, however, show an increased frequency of cerebrovascular ischemic events, related to a prothrombotic state. Coagulation disorder as a cause of stroke may be is associated with a deficiency, mainly of protein S (PS). [8]

Protein S is a vitamin K-dependent glycoprotein, which plays an important role in the regulation of blood clotting as a natural anticoagulant. [9] Synthesized by hepatocytes and megakaryocytes, it serves as a cofactor for the activation of protein C, thus inhibiting plasma and platelet factor V, as well as factor VIII. It also acts as a cofactor for the tissue factor inhibitory pathway inactivating factors Xa and tissue factor / factor VIIa. [10]

Protein S Deficiency (PSD) is a type of thrombophilia, which can be hereditary, with a varied pattern of gene changes, or acquired. Predisposes to a state of hypercoaguability that increases the risk of thromboembolic disease. [10]

Acquired PSD is not an uncommon disease and may be caused by a number of agents, such as age, sex, physiological hormone status, lipid metabolism, viral infections, acute or chronic inflammatory conditions, and therapy with vitamin K antagonists. The protein S circulates in the plasma at the concentration of 20-25mg L-1, 60% is bound to a protein of the complement

system - C4bBP - and only 40% remain in the free form. [10] The currently available tests for this protein measure the total and free plasma antigen and the functional PS. [10] The most of patients diagnosed with ischemic stroke present diseases, such as diabetes, hypertension, dyslipidemia, or cardiovascular disease. If these comorbidities are absent, a study of protein S should be carrying out in order to verify possible deficiency. [7]

In this case report, investigations were carried out to detect risk factors and possible causes of ischemic stroke, such as dyslipidemia, smoking, age, systemic arterial hypertension and family history, diabetes, autoimmune diseases, cardiovascular and hematological diseases, as well as to investigate obstruction by computed tomography of the left anterior choroidal artery. All these risk factors were eliminated, the cause being, therefore, indeterminate. Thus, protein S quantification was investigated through a biochemical test, identifying serum reduction of functional S protein. As the patient denied thromboembolism cases in the family, the deficiency of hereditary PS has been ruled out. It is believed, then, that this reduction of PS is acquired in this case. To understand the clinical findings of the patient, one must first understand the vascularization of the Anterior Choroidal Artery (AChA). AChA originates from internal carotid artery in the carotid cistern. Initially, it crosses the optic tract (OT) and, in the crural cistern, reaches the lateral margin of the cerebral peduncle. In the anterior part of the lateral geniculate body, the AChA crosses the OT and reaches the choroidal fissure (CF). AChA is divided into cisternal and plexual portions.

The branches of the cistern portion vascularize the structures: anterior and posterior perforated substance; OT; *globus pallidus*; *genus* and *crus anterius* of the inner capsule; pyriform cortex; uncus; amygdaloid nucleus; hippocampus; nucleus caudate; *substantia nigra*; red nucleus; subthalamus; ventro-anterior and ventro-lateral nuclei of the thalamus.

The branches of the plexus portion mainly vascularize the choroid plexus of the lateral ventricle. [11]

Therefore, occlusion of the choroidal artery causes, from the classic hemiplegia syndrome, hemianesthesia and hemianopsia due to the ischemic process of the infra and retrolenticular portions of the internal capsule, to asymptomatic cases due to an extensive network of collaterals arteries. [12] In this case, the patient presented central facial paralysis, hemiplegia and right hypoesthesia, since the occlusion occurred in the Anterior Left Choroidal Artery.

The treatment of patients with Venous Thrombo embolism associated with Protein S Deficiency only differs from those without thrombophilia in the duration of treatment. [13]Treatment consists of anticoagulation with unfractionated or low molecular weight Heparin initiated with Warfarin until the RNI reaches values between 2.0-3.0 on 2 consecutive days. [13] Heparin should be maintained for a period of at least 5 days to prevent skin necrosis, which is a rare phenomenon, but found early in the use of Warfarin in these patients with S protein deficiency. [13] Treatment should be maintained for at least 2 years. [14] Reports of cases involving cerebral ischemic events whose etiology was associated with Protein S deficiency presented divergent treatments, some opted for full anticoagulation throughout life, and other anticoagulation associated with antiplatelet aggregation. [15]

Conclusion

All patients with ischemic cerebrovascular accident less than 45 years of age, with no clear risk factors, should undergo serum tests to investigate S protein deficiency. There is also a need for further studies to define the best therapeutic course for patients with ischemic events due to Protein Deficiency S.

References

[1] Silva LLM, Moura CEMR, Godoy JRP. Fatores de risco para o acidente vascular encefálico. Universita Ciências da Saúde 2005; 03:145-160.

[2] Braga JL, Alvarenga RMP, Moraes JBMN. Acidente vascular cerebral. Ver. Bra. Med; 2003; 88-96.

[3] Radanovic M. Características do atendimento de pacientes com acidente vascular cerebral em hospital secundário. Arq Neuropsiquiatr; 2000; 58: 99-106.

[4] Maniva SICF, Freitas CHA, Jorge MSB, Carvalho ZMDFC, Moreira TMM. Vivendo o acidente vascular encefálico agudo: significados da doença para pessoas hospitalizadas. Rev. esc. enf. USP; 2013; 47(2).

[5] Tanaka AFD e Scheicher ME. Relação entre depressão e desequilíbrio postural em idosos que sofreram acidente vascular encefálico. Fisioter. Mov; 2013; 26(1).

[6] Zétola VHF, Nóvak EM, Camargo CHF, Júnior HC, Coral P, Muzzio JA, et al. Acidente vascular cerebral em pacientes jovens. Arq Neuropsiquiatr ; 2001; 59(3-B): 740-5.

[7] Neto JIS, Santos AC, Fábio SRC, Sakamoto AC. Infartos cerebrais em pacientes jovens relacionados à deficiência de anticoagulantes naturais. Arq. Neuropsiquiatr; 1996; 54(4): 590-4.

[8] Barinagrementería FA. Estados protrombóticos e isquemia cerebral. Arch. Inst. Nac. Neurol. Neurocir; 1993; 8(1): 5-8.

[9] Bereczky Z, Kovács KB, Muszbek L. Protein C and protein S deficiencies: similarities and differences. Clin Chem Lab Med; 2010; 48(1).

[10] Nogueira ASV. Factores que influenciam o doseamento da proteína S e consequente dificuldade de diagnóstico da deficiência hereditária desta proteína [dissertação]. Porto (Portugal). Instituto de Ciências Biomédicas Abel Salazar. Mestrado Integrado em Medicina, 2009.

[11] Ferreira A, Braga FM. Anatomia microcirúrgica da artéria coróidea anterior. Arq Neuropsiquiatr; 1990; 48(4): 448-453.

[12] Joaquim MAS, Honda PM, Pitelli SD, Almeida GM. Aneurismas da artéria coroideia anterior. Arq Neuropsiquiatr; 1987; 45(2).

[13] Ten Kate MK, Meer JVD. Haemophilia Protein S deficiency: a clinical perspective; 2008; 14, 1222–1228.

[14] Seligsohn U, Lubetsky A. Genetic susceptibility to venous thrombosis. N Engl J Med; 2001; 344: 1222–31.

[15] Amit Hooda, PD Khandelwal, Puneet Saxena. Protein S deficiency: Recurrent ischemic stroke in young. Ann Indian Acad Neurol; 2009; 12(3): 183–184.

Citation: **Marcelo José da Silva de Magalhães, Janniny Fernanda Lopes Mendes Figueiredo, Kelly Viviane Gomes Marques, Liliane de Oliveira Melo, Luciano Neto Loureiro Freitas, Moisés Figueiredo Camargos, Henrique Nunes Pereira Oliva**. *Stroke Associated with Reduced Protein S in Young Adult Brain: A Case Report. Archives of Neurology and Neuro Disorders. 2018; 1(1): 21-24.*