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What are the Rare Causes of Ischemic Stroke that I should know?

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Editorial

Ischemic stroke is defined as an acute neurological condition, caused by vascular obstruction that causes ischemia in a specific area of the brain, leading to physical and emotional sequelae [1-3].

It can be classified according to the TOAST Criteria in Acute Stroke Treatment according to its etiopathogeny in: atherosclerosis of great artery; cardioembolism (excluding cases attributed to the patent foramen ovale and interatrial communication); small vessel occlusion (lacunar); acute Ischemic stroke (AIS) of another etiology (determined); Ischemic stroke of undetermined etiology (two or more causes identified); Cryptogenic ischemic stroke [4,5]. Numerous modifiable and non-modifiable risk factors predispose ischemic stroke: systemic arterial hypertension (SAH), diabetes mellitus (DM), heart disease, dyslipidemia, smoking, alcoholism, obesity, sedentary lifestyle and family history of cerebrovascular events [4].

The Ischemic stroke has a peak of incidence between the 7th and 8th decades of life [6]. In young adults, it is a relatively rare entity, with less than 5% of cases occurring before 45 years of age [1]. The age limit for considering an AIS in an adult young people is still not defined, although most of the work includes patients up to 45 years of age [7]. Despite the better prognosis for patients over 50 years of age, the young person affected by this disease is subject to high morbidity and mortality rates. The AIS also damages society due to the years of productivity lost by the individual and the high financial costs of hospitalization and rehabilitation. [6-8].

The etiological spectrum of stroke in young adults is greater when compared to the elderly and requires extensive diagnostic investigation [7]. Other risk factors are described such as cervical-cephalic arterial dissections, primary and secondary vasculitis of the central nervous system, hematological and coagulation disorders (hyperfibrinogenemia, hemoglobinopathies, antiphospholipid antibody syndrome, C, S and factor V Leiden deficiency, among others), inflammatory and immunological diseases, and the use of illicit drugs [1,4,8].

Arterial dissections are among the causes of cerebrovascular infarction in young people under the age of 45, corresponding to 20% of the cases related to the age group [4]. The internal carotid artery is the most frequently affected, followed by the extra and intracranial vertebral artery respectively [4]. Paresis of a complex and heterogeneous group of angiopathies that develop under an influence of several genetic and environmental factors, for example Infection respiratory and oral contraceptives The diagnosis of dissection can be observed through ultrasound, angiotomography, angioresonance of cervical vessels, and the time of cerebral angiography by digital subtraction.

Vasculitis (or angeitis) of the CNS are serious, uncommon conditions that are difficult to diagnose [10]. It can be classified as primary CNS angiitis (PCNSA), when it occurs in isolation; secondary vasculitides are those in which vessel involvement is observed due to some systemic pathology, such as autoimmune disease, infections, neoplasias, drug exposure, among others. Currently, PCNSA is known to be a heterogeneous group, with granulomatous angiogenesis of

central nervous system (CNS) being the most common. This predominates in males and occurs in any age group. The diagnostic criteria for PCNSA include:

1. Presence of acquired neurological deficit and no definite explanation
2. Angiographic or histopathological findings of vasculitis in the CNS
3. Absence of other evidence of systemic vasculitis or other condition justifying these findings [10, 12].

The associated symptoms are chronic headache, encephalopathy, stroke / transient ischemic attacks (TIA) (usually recurrent), seizures, cognitive-behavioral changes, abnormalities focal sensory-motor, ataxia and myelopathy [10-12]. Regarding secondary vasculitis, cocaine and crack abuse, which is associated with an important part of cerebral vascular accidents, especially in young patients, should be highlighted [13]. Magnetic resonance imaging (MRI) and CT scan are not alone sufficient and specific for diagnosis [12]. Angiography has a better sensitivity than angioresonance in the involvement of small vessels, but both have low specificity for cerebral vasculitis [10-12]. CSF examination usually shows an increase in the number of leukocytes. When isolated lesions are observed, biopsy may be necessary to distinguish vasculitis from malignancies or other diseases [12].

Protein C is a serum protein dependent vitamin K and potentiated by the S protein [14]. In addition to a limiting action of the intrinsic coagulation pathway, protein C acts as an adjunct to the fibrinolytic system [14,15]. Congenital protein C in the homozygous form is incompatible with life [14]. In heterozygous patients, it usually raises the risk of thrombotic events from the second or third decade of life on trauma and surgeries [14,15]. Recently, it was found that the accidents thromboembolic events are more common when there is resistance to activated protein C than when there is a decrease in the total rate of protein C [14].

Protein S, a glycoprotein also dependent on vitamin K, is synthesized in the liver, megakaryocytes, osteoblasts and endothelium [16]. It is produced under the free (40%) and inactivated (60%) forms [14,16]. The deficiency of this protein can generate thromboembolic phenomena [6,14,16]. Some patients may have normal blood levels of total protein S and, even so, they are predisposed to vascular occlusion due to the decrease in their free form, a portion that has a greater action as a co-factor of protein C activated [14,16]. Its acquired deficiency is found in infectious states, neoplasms, nephropathies, pregnancy, the presence of tumor necrosis factor and other conditions [14]. In congenital deficiency, thrombosis may occur spontaneously or after trauma and infections [14,16].

Factor V is a key regulator in the initial phase of the blood coagulation cascade [14]. A small mutation in its gene (Leiden's Factor V) increases its action because it does not suffer a natural block of protein C, with the consequent installation of a state of hypercoagulability, which facilitates the formation of thrombi [14,17]. This mutation is present between 2% and 7% of the general population and in more than 50% of patients with a diagnosis of thromboembolism [14].

Homocysteine is a sulfur amino acid produced intercellularly by the demethylation of methionine [14,18]. Epidemiological evidence indicates that hyperhomocysteinemia is an independent risk factor for cerebrovascular disease [14,19]. the plasma concentration of homocysteine is influenced both by nutritional factors, such as folic acid status and levels of vitamins B6 and B12; life habits (smoking and alcoholism); renal, thyroid and atherosclerotic diseases; and by hereditary factors, especially linked to the enzymes of methionine and cysteine metabolism [14,18]. The reference value for plasma homocysteine stratified by sex is 6 to 12 μmol / L for women, and 8 to 14 μmol / L for men [18]. The morbid consequences are osteoporosis, mental retardation, lens luxation, and other organic changes, including vascular lesions and thrombosis [14,18]. Genetic hyperhomocysteinemia is an innate error in homocysteine metabolism due to the deficiency of one of the (B6, B12, folic acid), and in certain kidney diseases [14,18].

The presence of venous, arterial or small vessel thrombosis is a major feature of the antiphospholipid antibody syndrome (AFS) and the main cause of death in these patients [20]. Vessels of any caliber and from any site can be affected [20]. The most frequently reported events are deep venous thrombosis, pulmonary embolism and stroke [20,21]. Sneddon's syndrome is defined by the triad: ischemic stroke, livedo reticularis and positive antiphospholipid antibodies, generally observed in young patients [21,22].

A number of studies have been documented in the international literature suggesting an association between alterations in the interatrial septum, notably Patent Foramen Ovale (PFO), and ischemic stroke [5]. The oval foramen constitutes a communication hole between the right and left atria, which during the fetal circulation allows a shunt where most of the blood comes from the umbilical vein [23-25]. The oval foramen is considered patent when it is only functionally closed and not anatomical [26]. Immediately after birth, there is a decrease in pulmonary resistance and an increase in pressure on the left side of the heart, which leads to the closure of this orifice and the beginning of pulmonary ventilation [23,24]. Patients with this pathology are generally asymptomatic; however, PFO may lead to paradoxical embolism, resulting in cerebral or systemic events. [26,27]. This risk condition is more important in young people, since paradoxical embolism causes The present study considers the transesophageal echocardiogram associated with the bubble

test as the gold standard for the diagnosis and evaluation of PFO, although transcranial Doppler (TCD) is increasingly indicated. as an initial examination in the detection of right-left shunts [6,23,26].

Epidemiological studies have shown that hyperfibrinogenemia, independently of other factors, is associated with increased cardiovascular risk and the occurrence of thromboembolic phenomena [14,28–30]. Fibrinogen is a high molecular weight glycoprotein, synthesized by the liver, responsible for the formation of fibrin essential for platelet aggregation [14,30]. It acts on the modulation of endothelium function and promotes the migration and proliferation of smooth muscle cells, justifying the relationship between hyperfibrinogenemia and cardiovascular risk [14,30]. The plasma level of fibrinogen is between 1.8-3.5 mg / ml (185-350mg / dl) [32]. The Leiden Thrombophilia Study (LETS) showed that patients with plasma fibrinogen levels between 4-4.9mg / ml have a 1.6-fold higher risk for thrombotic events when compared to individuals in the reference category (<3mg / ml), while in people with serum levels ≥5mg / ml this risk is four The average life of fibrinogen is about 100 hours, during which it degrades slowly, losing atherogenic potential [30]. Because it also represents an important acute phase protein, in disease states (stroke, acute myocardial infarction myocardium, and deep venous thrombosis), it is difficult to say whether hyperfibrinogenemia is merely a biomarker or an etiological factor [14,29,30]. Levels of this protein may also increase with increasing age, smoking, hypertension and diabetes [29,31].

Regarding secondary vasculitis, cocaine and crack abuse, which is associated with an important part of cerebral vascular accidents, especially in young patients, should be highlighted [13] Magnetic resonance imaging (MRI) and CT scan are not alone sufficient and specific for diagnosis. Angiography has a better sensitivity than angioresonance in the involvement of small vessels, but both have low specificity for cerebral vasculitis. CSF examination usually shows an increase in the number of leukocytes . When isolated lesions are observed, biopsy may be necessary to distinguish vasculitis from malignancies or other diseases [10-12].

Hemoglobinopathies are associated with the occurrence of cerebrovascular events [34,40]. They are characterized by the presence of abnormal hemoglobin (Hb), due to a genetic defect that causes structural alteration of the beta chains of this protein [34,35]. Sickle diseases are referred to as whole of genetic diseases having Hb S combined with another mutant Hb (HbC, HbD or HbE) [34,36]. The term “Sickle Anemia” is reserved for the form of disease occurring in the homozygous SS. More rarely, hemoglobinopathy may still present as homozygous CC or as heterozygous AC (C-tract) [34,36,37]. The AVE is among the main clinical complications of patients with sickle cell disease [34,35,38]. S genotype homozygous (Hb SS - sickle cell anemia) is considered to be at higher risk than the SC and CC interactions [37,39]. Hb of red blood cells C have rhomboid crystals in their interior, are more viscous than normal and less deformable, and may cause an increase in peripheral resistance [38,39]. However, vaso-occlusion is not characteristic of the disease, as is the case with the C-carrier (HbAC) [37,38].

A study conducted by Napon C. et al involving patients with a previous stroke episode at the Yalgado Ouedraogo University Hospital, showed a prevalence of 62% of the AA genotype, 21% of the AC genotype, 15% of the AS genotype and 3 homozygous CC 40 patients. which does not seem to be a relationship between AC and AS traits, with a higher risk of developing ischemic stroke [40]. Although there is no direct association between hemoglobinopathy C and stroke, it may be suspected that fibrinogen would act as an additive factor, occlusion of blood vessels. Such a hypothesis may be based on the Poiseiulle Law which shows that blood flow is inversely proportional to viscosity [41-43]. Viscosity may be defined as the consequence of friction between adjacent layers of a fluid as they move relative to one another. [41,43]. In practical terms, this is what causes resistance to flow within a cylindrical tube such as the vessel Thus, a variable is a determinant of cerebral blood flow (CBF) and when elevated implies an increase in cardiovascular resistance (CVR) and reduction of the first one [43]. Coull BC et al state that chronic blood hyperviscosity is related to acute cerebral infarctions and present in individuals with risk factors for brain ischemia [44-49].

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