Moyamoya Disease: a case report in a 46-year-old Brazilian man

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ABSTRACT

Background: Moyamoya disease (MMD) is a rare pathology caused by a progressive unilateral or bilateral stenosis of the terminal portion of the internal carotid artery, leading to the development of collateral vessels. Case Presentation: We report a rare case of a 46-year-old male, born in the city of São Paulo, Brazil, with sudden muscular strength deficit and right hemiparesis, associated with headache and emesis. A priori, the initial diagnosis was arteriovenous malformation (AVM) after performing a series of complementary tests during the patient’s follow-up, also considering the clinical picture similar to that of Moyamoya disease (MMD). The conclusive diagnosis of MMD was finally established when the magnetic resonance imaging (MRI) showed a network of tortuous and dilated collateral vessels, with a hazy “smoke cloud” aspect with stenosis of the M1 segment of the middle cerebral artery (MCA), branch of the artery internal carotid artery (ICA). Conclusion: The recommended treatment was surgical revascularization with extracranial-intracranial bypass, with a favorable prognosis to the patient.

Keywords: Moyamoya disease; Internal Carotid Artery; Brain stroke; Pathophysiology; Revascularization

RESUMO

Introdução: A doença de Moyamoya (DMM) é uma patologia rara causada por uma estenose unilateral ou bilateral progressiva da porção terminal da artéria carótida interna, levando ao desenvolvimento de vasos colaterais. Relato do Caso: Relatamos o caso raro de um homem de 46 anos, natural da cidade de São Paulo, Brasil, com súbito déficit de força muscular e hemiparesia à direita, associado a cefaleia e vômitos. A priori, o diagnóstico inicial era de malformação arteriovenosa (MAV) após a realização de uma série de exames complementares durante o seguimento do paciente, considerando também o quadro clínico semelhante ao da doença de Moyamoya (DMM). O diagnóstico conclusivo de DMM foi finalmente estabelecido quando uma ressonância magnética (RM) mostrou uma rede de vasos colaterais tortuosos e dilatados, com um aspecto nebuloso de “nuvem de fumaça” com estenose do segmento M1 da artéria cerebral média (ACM), ramo da artéria carótida interna (ACI). Conclusão: O tratamento recomendado foi a revascularização cirúrgica com bypass extracraniano-intracraniano, com prognóstico favorável ao paciente.

Palavras-chave: Doença de Moyamoya; Artéria Carótida Interna; Infarto cerebral; Fisiopatologia; Revascularização

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Moyamoya disease (Moyamoya disease) is a rare disease characterized by progressive unilateral or bilateral stenosis of the terminal portion of the internal carotid artery, of unknown etiology\(^1\). In addition, there is the angiogenesis of abnormal collateral vessels in the nuclei of the base, as a form of compensation caused by the ischemia of the regions affected by the pathology\(^4\).

The first case was described in 1957 and was established by Suzuki and Takaku in 1969, the main clinical manifestation of the disease being the stroke in its ischemic and hemorrhagic forms\(^1\). Recent studies indicate that the amount of collateral vessels at the base of the skull serve as markers of disease severity and degree of progression\(^4\).

Moyamoya is a Japanese term that means “cloud of smoke”, since, in arteriography, the network of collateral vessels formed at the base of the skull is very visible and characteristic\(^1\). In epidemiology, East Asia dominates in matters of the prevalence of cases, because of the presence of a genetic polymorphism in this population of Koreans and Japanese that confers the pathogenesis of the disease\(^3\).

The prevalence peaks in ages are around 10 years and between 30 and 45 years. Clinical symptoms include ischemic stroke and transient ischemic attack (TIA)\(^5\), with a prevalence rate of 50 to 75%, and intracerebral hemorrhage (10 to 40%), more common in adults than in children\(^3,6\).

The gold standard in the current diagnosis of Moyamoya disease is cerebral angiography. As it is an invasive exam, we can use other methods such as angiotomography and MR angiography, which are non-invasive exams. Currently, there is no specific treatment to prevent the progression of Moyamoya disease. However, the procedure predilection for patients with ischemic and hemorrhagic strokes is surgical revascularization (extracranial-intracranial bypass)\(^6,7\).

The following study aims to present a clinical case of Moyamoya disease that occurred in Brazil and, from there, carry out a review of the pathophysiology, epidemiology, clinical presentation, diagnosis and treatment of this disease.

**Case Presentation**

Male patient, 46 years old, born in São Paulo, was admitted to the emergency room of a reference hospital in the city of São Paulo on October 16, 2019, complaining of headache and emesis 1 hour before. A thorough physical examination and anamnesis were carried out, in which the patient denied a pathological history, allergies and previous surgeries. He had a regular general condition and was hemodynamically stable, eupneic in room air, conscious and oriented in time and space, in addition to the Glasgow Coma Scale score of 15.

Hemiparesis was observed on the left, with grade IV muscle strength (against strong resistance), according to the Medical Research Council score. The neurological examination demonstrated preserved normoactive reflexes, sensitivity and coordination. A computed angiotomography of the skull with iodinated contrast was then performed (Figures 1 and 2), which showed a tangle of vascular structures 2.0 cm long at the level of the proximal portion of the M1 segment of the right middle cerebral artery (MCA), in the region of the insular limb, accompanied by a hyperdense lesion in the nuclei of the right base, which indicated adjacent intraparenchymal hemorrhage with flooding of the ipsilateral ventricle.

The correlation between clinical data and the complementary examination suggested the diagnosis of arteriovenous malformation (AVM) (ICD10: Q28.2), since the headache and vomiting clinic and the AVM-compatible imaging test were hypothetical for this pathology. The next day, a cranial tomography was performed to follow the progress of the lesion (Figure 3), in which a hematic component with resorption aspect was observed in the right posterior ventricular region, where a minimal extension of this component to the ventricular and plexus system was highlighted. There were also foci of signal alteration in the brain white matter,
characteristically ischemic, related to gliosis. The other areas of the brain parenchyma showed signs of retractive involvement with marked differentiation between the gray and deep white substances (leukomicroangiopathy). Thus, such conditions caused an adaptation in the cortical grooves, fissures and in other liquoric spaces, which were widened diffusely.

Under analgesia, over the days, the patient evolved with total headache improvement, without neurological deficit, and muscle strength was restored to Grade V. However, vomiting persisted until October 28, 2019, when an angiography was performed with access to the right internal carotid artery (ICA) with a 6F diagnostic catheter through femoral puncture. It was reported that a small dilation of about 2.0 x 0.4 cm, at the margin of the vascular enamel, in capsule-nuclear topography was observed, originating from the M1 segment of the right MCA, which led the diagnosis to proceed as an AVM. After days, a CT of the skull was performed on the patient, which showed, in the nuclei of the base on the right, a lesion suggestive of infarction, with tissue death resulting from a stroke (Figure 4).

An endovascular treatment for AVM has been proposed. Thus, an MRI was performed on November 4, 2019 to confirm the AVM, using the T1-, T2-weighted sequences (Figure 5), and diffusion and FLAIR sequences. Flow-sensitive 3D-TOF sequences were also performed (Figure 6). Vascular veinage was reported close to the proximal portion of the M1 segment of the right MCA, measuring about 2.0 x 1.5 cm, in addition to intraparenchymal hemorrhage with mild gliosis, located in the region of the radiated crown and posterior capsular
nucleus on the right. The remaining portions of the M1 and M2 segments of the right MCA tapered, while there was no significant stenosis in segments A1 and A2 of the anterior cerebral arteries (ACAs), the segments M1, M2 and M3 of the left middle cerebral artery, the P1, P2 and P3 of the posterior cerebral arteries (ACPs), and intradural segments of the vertebral arteries, as well as in the basilar artery. In the T2-/FLAIR sequences, there were rare outbreaks of hypersignal, which characterized the local infarction, which ended up suggesting the diagnosis of AVM.

After 23 days, the patient was referred for a control cerebral angiography (Figures 7 and 8) as part of the investigation of the hemorrhagic focus. In the image examination, the presence of proliferation of lenticular arteries stretched to the right, large and tortuous was reported. It was also noted tortuosity and stenosis of the M1 segment of the right MCA (which differs from the AVM, which is generally not associated with the decrease in the caliber of the great vessels of the base), near the origin of these perforating branches, with a slowed circulatory time in the more distal segments of this artery, whose territory has also been opaque in a retrograde manner by pial branches from the ipsilateral ACA and ACP.

The cloudy aspect in the “smoke cloud” in the image was reported and, in addition, the presence of nidus, characteristic of AVM, was not observed, or arteriovenous fistula, nor the large drainage veins also characteristic of arteriovenous malformation (AVM). Thus, the diagnosis of Moyamoya disease (ICD-10: I67.5) was established and the immediate neurosurgical approach to revascularization by extracranial-intracranial bypass was considered, in order to prevent further ischemic and hemorrhagic stroke injuries.
The surgery called STA-MCA was performed through a microscope, using a micro-anastomosis technique, in which the "donor vessel", the superior temporal artery (STA), which irrigates the scalp, was resected and connected to the right MCA (right internal carotid artery branch) in order to divert blood flow to the region of the collateral vessels typical of the pathology. After neurosurgery, the patient was kept under monitoring of vital signs and then a skull CT scan was performed (Figure 9) to assess the prognosis, which by the way was favorable, considering that only a hypodense area of inaccurate limits was observed, capsulonuclear and in the semi-oval center on the right, but without any evident atrophy or expansion. The cortical grooves, cisterns and brain ventricles were normal and with preserved morphology and dimensions, and the patient did not present any weakness due to well-fixed surgery.

Figure 7. Brain angiography of intracranial view in profile showing tortuosity and stenosis of the M1 segment of the distal MCA of the ICA (blue arrow). No drainage veins are observed.

Figure 8. Cerebral angiography of intracranial incidence in AP showing the "smoke cloud" (black arrow) in the region of the right portion, in addition to the tortuosity and stenosis of the M1 segment of the MCA (orange arrow).

Figure 9. Skull CT in axial section after revascularization surgery. Note a favorable prognosis, without signs of density resulting from hemorrhage nor infarction outbreaks of ischemic origin.
Patients with Moyamoya disease (MMD) have a peculiar progressive unilateral or bilateral stenosis of the terminal portion of the internal carotid artery and the consequent formation of abnormal collateral vessels in the nuclei of the base, which compensates for the ischemia of the affected areas, where the “cloud of smoke” apparent in arteriography is due to the formation of these vessels.

It was first described by Suzuki and Takaku, however it is probably more common than the literature suggests. There is a higher incidence in Koreans and Japanese people due to the presence of a genetic polymorphism. The disease has a higher prevalence in children up to 10 years old (50% of cases), with the remainder between 30 and 45 years old, with greater involvement in women.

The Japanese term “Moyamoya” means something nebulous, due to the angiographic findings that are a diagnostic criterion.

The arteries of the Willis polygon progressively occlude. The main clinical manifestations of the disease are ischemic and hemorrhagic stroke, the latter being the most common form in adults, with repercussions such as recurrent transient ischemic accidents (TIAs), epileptic seizures, decreased level of consciousness, hemiparesis, speech disorders, sensitivity, choreic movements of the face and limbs and headache.

The main difference between children and adults is precisely the dissimilar repercussion of the type of stroke, which in children is predominantly ischemic, while in adults, hemorrhagic. This is due to long-term hemodynamic stress in very small moyamoya vessels, in addition to arteriosclerotic changes in adults, which facilitates the formation of microaneurysms, which does not occur in children, since the vessels are more flexible and non-sclerotic. Interestingly, the angiography of these age groups does not have significant changes, based on the angiographic classification of Suzuki and Takaku (Table 1), in which most are part of stage III, where stenosis or occlusions in the anterior circulation are already observed, with greater prominence. collateral vessels. This particular patient presented stage III.

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<tr>
<th>Table 1. Angiographic classification (according to Suzuki and Takaku, 1969)</th>
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<td>I. Stenosis of the carotid artery in its suprasellar portion, usually bilateral</td>
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<td>II. The moyamoya vessels begin to develop at the base of the brain</td>
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<tr>
<td>III. The moyamoya vessels become more prominent as the main trunks in the anterior circulation become severely stenotic or obstructed</td>
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<tr>
<td>IV. The posterior cerebral arteries are clogged, the moyamoya vessels begin to narrow and the collateral routes of extracranial circulation develop</td>
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<tr>
<td>V. The moyamoya vessels are reduced and extracranial circulation progresses</td>
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<tr>
<td>VI. The moyamoya vessels and the main cerebral arteries disappear completely, the cerebral hemispheres receive blood through the abnormal extracranial-intracranial anastomosis</td>
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Of unknown etiology, it is a fact that the disease has predisposing factors such as age and ethnicity, associated with infections and toxins which can favor pathogenesis. Due to a genetic expression, the differences between adult American and Japanese carriers are notable, since ischemias are more prevalent in the former, in contrast to the latter, who have hemorrhagic infarctions. This is due to the deficiency of plasminogen type II, which is associated with the replacement of human leukocyte antigen 601 (HLA-601) of tyrosine, which predisposes to thrombosis. In a study of HLA class II genes involving 71 samples, it was observed that the heterodimer DQB1*0502 did indeed have an association with Moyamoya disease. In this patient, it is interesting to highlight his ethnicity, since he is not Asian descendant, whose population has much greater risks of developing the disease due to the glaring genetic predisposition.

Structurally, the lesion due to stenosis and occlusion of the arteries is made possible by fibrocellular thickening of the arterial intima, with hypertrophy of smooth muscle cells that migrate to the middle layer, in addition to proliferation of the intimate layer, which may occur in response to the involvement of the vessel wall. In addition to intracranial vessels, the disease also involves systemic vessels, and this includes the superficial temporal artery. According to studies, it represents a type of collateral circulation which develops due to cerebral hemodynamics due to compensatory changes in the blood flow of the cerebral parenchyma, as a way to prevent loss of function and thus avoid possible neurological sequelae.

Regarding the case report, the exclusion of the differential diagnosis of arteriovenous malformation (AVM) should be emphasized due to the fact that there are no drainage veins in Moyamoya disease, no matter how much the clinical picture and the skull CT, angiography, angioresonance and angiotomography of both are similar, besides no void flow (intense flow characteristic of AVM in MRI) and nidus (nest of collateral vessels with dilation also characteristic of AVM). Table 2 presents the diagnostic guidelines for MMD, however, the patient did not present bilateral findings, which made it difficult to conclude.

In relation to the skull CT angiotomography after intravenous contrast, a hyperdense lesion was observed with evident hemorrhage in the nuclei of the right base. In addition, intraparenchymal hematoma was investigated using cerebral angiography, with the femoral puncture technique. It was a conclusive diagnosis, since satellite dilation was observed at the margin of the apparent vascular enamel, with the presence of tortuous collateral vessels in a cloudy aspect, which do not exist in the AVM.

### Table 2. Diagnostic directors for Moyamoya Disease (according to MHWJ)^7^

| I. | Stenosis or occlusion of the intracranial internal carotid artery or adjacent anterior and middle cerebral arteries |
| II. | Abnormal vascular network adjacent to the stenosed artery identified during the arterial phase of angiography |
| III. | Bilateral findings on angiography |
| IV. | No other identifiable cause |

The treatment for Moyamoya's disease is, in most cases, surgical, and the standard procedure is surgical revascularization in cases of stroke, which has a preventive effect of possible recurrences, as it increases cerebral hemodynamics, while in cases of patients with stroke that have rebleeds, this procedure has still been debated regarding the effectiveness. The most used type of surgical revascularization is the extracranial-intracranial bypass, with
reinforcement of indirect synangiosis to consolidate a future vasculogenesis, and these have the purpose of transporting the blood flow from the internal to the external carotid system.\(^6,9\) Regarding the administration of antiplatelet drugs, there is weak scientific evidence that recommends patients with ischemic symptoms, and is not recommended for patients with hemorrhagic or asymptomatic onset.\(^9\)

A technically easy indirect revascularization is the brain-hard-arteriosinangiosis, which consists of transplanting a scalp artery with a fragment of epicranial aponeurotic galea through an osteoplastic craniotomy, with a linear dural opening. The good prognosis and success of neurosurgery depends exclusively on the patient’s natural neovascularization capacity.\(^6,12,13\) However, a study showed that the patient’s age affects the development of collateral vasculogenesis when indirect bypass, so the direct bypass treatment is, in fact, the gold standard for the treatment of MMD.\(^14,15\) In patients with hemorrhagic Moyamoya disease, the combination of direct bypass to indirect is the one with the best prognosis, according to a survey of a conclusive prospective study involving 113 hemorrhagic patients.\(^5\)

The most used extracranial-intracranial approach is performed by means of low flow micro-anastomosis of the superficial temporal artery (STA) with the middle cerebral artery (MCA), called STA-MCA, using a microvascular technique, through a microscope, in order to establish the deviation of blood flow to the diseased region, where the collateral vessels are located. Such cerebral revascularization procedure is contraindicated in cases of decompensated coagulopathy. In the procedure, the STA, which irrigates the scalp, is resected. Further, a craniotomy is performed in search of the MCA (branch of the internal carotid artery), which is arteriotomized to be anastomosed with the STA. Temporary clips are used in the MCA, in order to avoid a hemorrhagic condition during arteriotomy.\(^1,3,7,8,14\)

CONCLUSION

Our case highlights the importance of a good diagnosis for MMD, considering that it was initially confused with AVM when having the clinical and imaging diagnosis in mind. Upon thoroughly evaluating the diagnostic criteria and imaging exams, the case was elucidated, and the patient underwent a successful STA-MCA bypass surgery.

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