

Moyamoya disease: a review with emphasis on its surgical treatment

Enfermedad de Moyamoya: una revisión con énfasis en su tratamiento quirúrgico

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Resumen

La enfermedad de Moyamoya (EMM) se caracteriza por la estenosis progresiva y la oclusión de las arterias carótidas internas en la base del cráneo. Se observó por primera vez en 1957 por Takeuchi y Shimizu en arteriografías anormales del cerebro. Esto representa el 6% de los accidentes cerebrovasculares en los niños, y es una enfermedad cerebrovascular importante en este grupo de edad en Japón. La mayoría son casos esporádicos de la EMM, pero hay también una variante familiar que se produce en aproximadamente el 8% de las veces. El tratamiento de la EMM depende de la presentación clínica del paciente y la etapa de la enfermedad. Las opciones de tratamiento incluyen la observación y el seguimiento, el tratamiento médico y el tratamiento quirúrgico, o incluso combinaciones de ellos. En general, no existe una recomendación establecida en relación con la gestión de la enfermedad, una vez que hay una ausencia de estudios prospectivos aleatorizados con seguimiento razonable. En este artículo realizamos una revisión de la literatura acerca de la EMM, con énfasis en su tratamiento quirúrgico.

Palabras clave: Enfermedad de moyamoya, trastornos cerebrovasculares, procedimientos neuroquirúrgicos.

Abstract

Moyamoya disease (MMD) is characterized by progressive stenosis and occlusion of the internal carotid arteries at the base of the skull. It was first observed in 1957 by Takeuchi and Shimizu in abnormal arteriograms of the brain. It accounts for 6% of strokes in children, and it is a major cerebrovascular disease in this age group in Japan. Most are sporadic cases of MMD, but there is also a familiar variant that occurs in approximately 8% of the times. The treatment of MMD depends on the patient's clinical presentation and the stage of the disease. Treatment options include observation and monitoring, medical treatment and surgical treatment, or even combinations of them. In general, there is no established recommendation regarding the management of the disease, once there is an absence of prospective randomized trials with reasonable follow-up. In this article we perform a review on the literature about the MMD, with emphasis on its surgical treatment.

Key words: Moyamoya disease, cerebrovascular disorders, neurosurgical procedures.

Introduction

Moyamoya disease (MMD) is characterized by progressive stenosis and occlusion of the internal carotid arteries at the base of the skull, including its proximal branches. This process is followed by the formation of an extensive network of dilated collateral vessels, which determines angiographic appearance of "smoke cigarette", whose Japanese term is moyamoya. This fragile collateral network develops as a consequence of the chronic hypoxia of the brain¹.

In addition, some authors² report the difference between MMD and Moyamoya syndrome (MMS). The latter is associated with other known conditions that may be a risk factor for disease development, including the type I neurofibromatosis, Down syndrome and sickle cell anemia. Patients with unilateral involvement are also recognized as having MMS. However, up to 40% of cases, involvement becomes bilateral^{3,4}. Another important risk factor is previous exposure, in predisposed persons, to cranial radiotherapy to treat brain tumors. In our reality, this disease has a rare incidence, according national studies⁵⁻¹³, mainly in the non-Asian population.

Objective

The purpose of this paper is to perform a review of current literature regarding the moyamoya disease, with emphasis on its surgical treatment.

Methods

A review of the literature was made based on articles from the databases of MEDLINE and SCIELO, using the "Moyamoya" keyword. References of the same were tracked once the articles were found. Some other articles related to the topic were also included in the study.

The result of the research was analyzed and shown in this paper. A discussion of the topic was made, having the aim of answering the initial doubts that motivated the review.

Discussion

Epidemiology

MMD was first observed in 1957 by Takeuchi and Shimizu¹⁴ in abnormal ar-

teriograms of the brain. In 1969 it was characterized and defined by Suzuki and Takaku¹ and was initially called "carotid's hypoplasia". It is a rare condition, with a marked prevalence in Asian countries like Japan and Korea.

It accounts for 6% of strokes in children, and it is a major cerebrovascular disease in this age group in Japan. Most are sporadic cases of MMD, but there is also a familiar variant that occurs in approximately 8% of the times¹⁵. First, this disease was supposed to be exclusive of persons whose origins go back to Asia, especially Japan, however, in recent studies, the MMD is already present in various ethnic groups throughout the world, including South American and European people¹⁶. It has a bimodal peak of incidence, one in childhood, around five years and another in adulthood, around the fourth decade of life¹⁷. Moreover, it is more prevalent in women with an incidence of 1.8 to 2 higher than men. In Japan, it has an annual prevalence around 3 cases per 100,000 children¹⁶. In Europe, it has a prevalence of about one tenth of that observed in Japan¹⁸.

Etiology and Pathogenesis

Not yet fully elucidated, the pathogenesis of MMD is associated with chronic deposition of smooth muscle fibers in the vascular wall, associated to the presence of a chronic local inflammatory response, whose evolution leads to a progressive occlusion of intracranial vessels. Also, it must take into account the role of vascular growth factors, especially fibroblast growth factor type β , involved in the neovascular response as mentioned by Hojo et al¹⁹. Recently, in 2008, a genetic locus associated with the mutation on chromosome 17, 17q25, was associated with a MMD with an autosomal dominant pattern, in which there is a change in tissue inhibitor of metalloproteinase type 2 (TIMP-2)²⁰.

Pathology

The initial lesion occurs primarily in the intimal layer of the cerebral vessels. There is deposition of fibers and a progressive stenosis of the vessel lumen. The internal elastic layer becomes tortuous and it is also noted a local inflammatory response. As the occlusion of major intracranial vessels occurs, there is therefore the installation of a chronic state of cerebral ischemia. This fact determines the development of an extensive network of collateral fragile vessels that involves

the base of the brain. These vessels are dilated and tortuous, and their internal elastic layers are discontinuous and followed by areas of fibrosis in the tunica media. This capillary fragility contributes to the formation of micro aneurysms that predisposes bleeding events during the course of the disease¹.

Clinical Presentation

The progressive stenosis of the internal carotid and its main branches determines a state of chronic brain oligoemia, partially compensated by a fragile network of collateral vessels. When there is an insufficient cerebral blood flow, the installation of cerebrovascular events occurs. These events can be transient ischemic attack (TIA) or established strokes. In infants, these episodes may be triggered by crying, coughing or even during the execution of wind instruments, as well as during a systemic disease with dehydration. These events may provide a rich list of symptoms, which may include epileptiform events, as well as headache, visual disturbances, paresis, sensory deficits, movement disorders, progressive cognitive deterioration, and even psychiatric symptoms⁵.

In adults, symptoms may be attributed to bleeding events, although in this age group ischemic presentations are also common¹⁸. Such events are attributed to hemorrhagic rupture of collateral vessels in patients who have undergone long periods of hemodynamic stress, and are often accompanied by cerebral aneurysms. Among the localizations of brain aneurysms, they are frequently on the top of the basilar artery and in the emergence of the posterior communicating artery².

Usually the bleeding simulates a hemorrhagic bleeding hypertensive fashion, affecting mainly the basal ganglia and thalamus. It can also present with intraventricular bleeding and even with meningeal hemorrhage. Another aspect of the clinical presentation is the considerable presence of headache, which can mimic a migraine crisis, which is summarized in the pathophysiology of dilated leptomenigeal vessels that stimulate dural nociceptors²¹. It may become persistent even after revascularization, in 63% of the cases²¹. Moreover, it is possible to develop choreic movements due to dilatation of moyamoya vessels in the basal ganglia, especially in children, with a regression rate of around 80% after successful revascularization²². There are

also possible ophthalmologic findings related to the MMD during examination of the fundus, the so-called “morning glory disc”, that is the increase of the optic disc associated with retinovascular changes²³.

Diagnosis

MMD must be considered especially in children presenting with acute neurological deficits, and in those patients with a previous diagnosis of associated conditions. It must take into account that delayed diagnosis and delayed treatment expose patients to risk of permanent brain injury². The diagnosis is made based on radiological findings, especially arteriography of cerebral vessels, and clinical criteria for inclusion and exclusion. To this end, a guideline was defined by a team of experts from the Ministry of Health of Japan that includes: stenosis or occlusion of the terminal portion of the internal carotid or proximal portions of the anterior or middle cerebral artery, abnormal collateral network in the vicinity of stenotic vessels, bilateral findings and no other identifiable cause for such findings⁶.

Computed tomography

In patients with established diagnosis of cerebral ischemic events are common areas of hypodensity in regions of the basal ganglia and “watershed” areas².

Magnetic Resonance Imaging (MRI)

Regions in acute cerebral ischemia can be well documented with images of diffusion-weighted sequences, while old infarcts are best seen on T1 and T2-weighted images. The reduction of cerebral blood flow in cortical areas can be spotted by FLAIR sequence in which there is a hyper intense signal outlining cortical sulci, called the “ivy sign”. Moreover, the reduction of “flow voids” in regions of the internal carotid artery (ICA), anterior cerebral artery (ACA) and medium cerebral artery (MCA) associated with an increase in collateral vessels of the basal ganglia and thalamus is considered essential to the diagnosis. However, it must be noted that although MRI can establish the diagnosis, it lacks information essential to treatment planning, especially regarding the surgical strategy⁸.

Angiography of cerebral vessels

The basis of diagnosis is arteriography of cerebral vessels. In addition, it offers a

Table 1.
Arteriographic grading system of Suzuki and Takaku¹

Grade	Definition
I	Narrowing the apex of the ICA*
II	Incipient moyamoya vessels
III	Progressive stenosis of the ICA and intensification of moyamoya vessels
IV	Development of collaterals from the ECA**
V	Intensification of ECA collaterals and reduction of moyamoya vessels
VI	ICA occlusion and disappearance of moyamoya vessels

*ICA: internal carotid artery; **ECA: external carotid artery.

staging of MMD as proposed by Suzuki and Takaku¹ (Table 1).

Other diagnostic methods

The electroencephalography (EEG) may show specific findings, especially in pediatric patients. These findings include a slowing at the posterior cerebral and centro temporal regions with a pattern of monophasic slow waves induced by hyperventilation²⁰.

Moreover, studies of cerebral blood flow contribute to setting standards pre-and post-intervention and quantify response to treatment of cerebral revascularization. Such methods include transcranial doppler, cerebral perfusion computed tomography, positron emission tomography (PET), MRI with brain perfusion and single photon emission tomography (SPECT) with acetazolamide overload². The natural history of the MMD is variable with a pattern of evolution very slow to events quickly installed and neurological decline. It is estimated that over two thirds of patients have symptomatic progression within 5 years, and the outcome is poor without treatment. In contrast, after revascularization treatment, the estimated progression rate is of around 2.5%²⁴.

Treatment modalities

The treatment of MMD depends on the patient's clinical presentation and the stage of the disease. Treatment options include observation and monitoring, medical treatment and surgical treatment, or even combinations of them. In general, there is no established recommendation regarding the management of the disease, once there is an absence of prospective randomized trials with reasonable follow-up²⁰.

Clinical

Can be based on the use of vasodilators, anticoagulants, antiplatelet agents, anti-convulsants, but still, there is no definitive recommendation regarding its use². Moreover, it is not the focus of this study.

Surgical

The goal of surgical treatment is to promote effective and lasting revascularization of the brain parenchyma, in order to prevent ischemic events over the course of the disease. Moreover, with the relief of cerebral ischemia, it is believed that there is a decrease in network fragile collateral vessels and thereby a reduction on the risk of bleeding events, during adulthood. Overall, revascularization procedures can be grouped into two groups, namely the direct and indirect one.

In fact, the first attempt of surgical treatment for this disease was proposed by Suzuki and Takaku¹. They have tried to promote a greater dilation of cerebral vessels and consequent increase in blood flow through sympathetic denervation of the carotid system through the superior cervical perivascular gangliectomy and superior cervical sympathectomy. However, despite good initial results, it has failed to prevent disease progression.

Direct revascularization

In this modality of treatment, there is the construction of a bypass between the external carotid artery and ICA through its terminal branches, which can be MCA or ACA. These anastomoses may be low or high flow. In the low-flow bypass the superficial temporal artery (STA) is anastomosed to a cortical artery (Figure 1). In the high-flow bypass a saphenous vein

graft is created between the external carotid artery and a cortical artery (Figure 2). This method increases cerebral blood flow soon after the procedure and, in principle, should be the method of choice.

However, this technique can be difficult to implement and even impossible, especially in children where the caliber of the vessels is the main limitation. Moreover, the need for temporary clipping of a cortical vessel may not be well tolerated in a brain already ischemic, and can determine definitive brain injuries².

With the introduction of microsurgical techniques, the first direct revascularization was performed by Yasargil and Donaghy²⁵ in 1967, as reported by Ishii et al²⁶, with good results, followed by the diffusion and use of microsurgical technique over the years.

Indirect revascularization

It involves a confection of a flap of vascularized tissue by the external carotid artery (ECA), which can be pericranium, dura mater, temporal muscle or even a branch of TSA over the cortical surface, in direct contact with the pia mater, in order to stimulate angiogenesis on the cortical brain surface. It includes encephaloduroarteriosinangiosis (EDAS), encephalomyosinangiosis (EMS), omental transposition (no longer in use) and trepanations without sinangiosis. These methods are based on the known fact of the brain tissue capacity of developing angiogenesis in the presence of a state of ischemia²⁴ (Figure 3).

In this sense, Karawasa et al²⁷, in 1977, described the EMS, in which the inner surface of the temporal muscle was neared to the brain surface. This technique reduced the number of TIAs and strokes, but ended an increased risk of developing seizures and subdural collections.

In 1981, Matsushima et al²⁸, proposed the EDAS, in order to decrease the complications inherent in previous technique. In this procedure, the TSA was isolated and neared to the surface of the brain followed by its attachment to the edges of the dura mater. The follow-up of their patients showed a trend toward reduc-

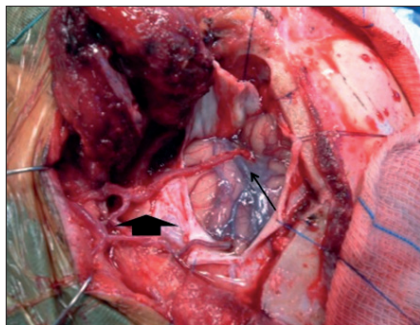


Figure 1. "By-pass" low-flow between the STA (head arrow) and MCA (M4 segment) (arrow) at the left side in a patient with moyamoya disease (Source: Dr. Juan Antonio Flores Castro).

tion of ischemic events and maintenance of cognitive function. Nevertheless others investigators could not reproduce the results reached by Matsushima.

In the evolution of knowledge about this disease, many suggest that the failure of EDAS during attempts to reproduce the work of Matsushima et al²⁸, was the fact that they had not created an actual interface between the TSA and the brain surface, since the arachnoid membrane and pia mater were intact²⁸. With the opening of these membranes, called sinangiose pial, the development of collaterals was more effective.

Among the surgery's complications, the most feared is the development of stroke during the perioperative or postoperative time, which is common in children, since the induced hyperventilation during crying may promote cerebral vasospasm as a result of hypocapnia. Other complications include the possible development of acute or chronic subdural collections, especially when the involvement of the temporal muscle².

Conclusion

The moyamoya disease is a rare condition that affects usually people of Asiatic origin. Its pathophysiology is still not fully understood, but it involves a chronic inflammatory response whose evolution leads to the progressive occlusion of intracranial vessels. Its management



Figure 2. Postoperative arteriography after bypass between ECA and MCA at the right side with high-flow saphenous vein graft (arrow). Note adequate opacification of the cortical territory of the MCA and patency of the bypass (Source: Dr. Juan Antonio Flores Castro).

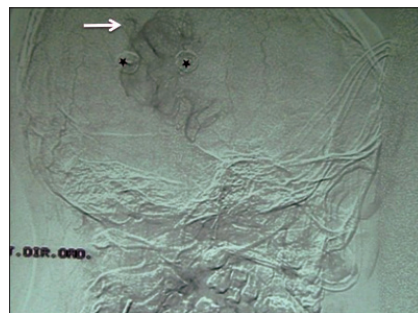


Figure 3. Capillary time of angiography reveals vascular blush at the superior parietal region showing local angiogenesis (arrow) after EDAS. Note trepanations at the edges of the craniotomy (star) (Source: Dr. Juan Antonio Castro).

is involves the use of medications, but mainly needs some kind of revascularization techniques, which, due to their complexity, are not performed on most of the service.

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