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MOYAMOYA DISEASE

REPORT OF THREE CASES IN BRAZILIAN PATIENTS

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ABSTRACT - Moyamoya disease (MMD) is a chronic occlusive cerebrovascular disease of unknown etiology reported mainly in the Japanese. Most cases occur in children. The disease is rare in non-Oriental adults manifesting itself mostly as intracerebral hemorrhages. We describe MMD in 2 non-Oriental young adults and one adolescent that developed cerebral infarctions. The adults were medicated with aspirin and no medication was given to the adolescent. All patients did not deteriorate in a follow-up period from 1 to 4 years. Although rare, MMD is an important cause of stroke in young individuals and may well be underreported: only 18 patients have been reported till 1997 in Brazil. Neurologists should include MMD in differential diagnosis of ischemic and hemorrhagic strokes in young adults.

KEY WORDS: moyamoya disease, adult, chronic occlusive cerebrovascular disorder, stroke.

Doença de Moyamoya: relato de três pacientes brasileiros

RESUMO - A doença de moyamoya (DMM) é patologia cerebrovascular oclusiva crônica de etiologia desconhecida, descrita inicialmente em japoneses. A maioria dos casos ocorre em crianças. Relatamos três casos de DMM, dois adultos e um adolescente não-orientais que apresentaram a forma isquêmica da doença, embora adultos apresentem principalmente a forma hemorrágica. Todos foram submetidos a tratamento conservador e acompanhados durante um a quatro anos, sem piora ou recorrência dos déficits neurológicos. A DMM é uma incomum mas importante causa de acidente vascular cerebral isquêmico, sendo subdiagnosticada em nosso país, onde apenas 18 casos foram descritos até o 1997.

PALAVRAS-CHAVE: doença de moyamoya, adulto, doença cerebrovascular, acidente vascular cerebral.

Moyamoya disease (MMD) is a rare and chronic occlusive cerebrovascular disorder of unknown origin mainly reported in the Japanese. Most cases occur in children[1-4]. Increasing numbers of cases are now being reported in non-Japanese adults[2]. Characteristic angiographic findings were first described in Japan by Takeuchi and Shimizu in 1957,[4] according to Ueki et al.[4]. It is an unusual but important cause of stroke[2,5]. Initially, it is characterized by progressive stenosis or occlusion at the distal ends of the bilateral internal carotid arteries (ICAs) that subsequently may progress to involve both the middle cerebral artery (MCA) and the posterior cerebral arteries[3,6]. An abnormal capillary network which develops at the base of the brain and is considered as a secondary collateral system formed as a result of progressive ischemic changes. This abnormal vascular network is called moyamoya vessels (MV), "moyamoya'' being a Japanese word that means "something hazy,

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like a puff of smoke drifting in the air", describing the angiographic picture that they present[3]. Usually, MMD manifests by signs and symptoms of cerebral ischemia or infarction in childhood due to impaired circulation partially restored by collateral channels. However, adults tend to present cerebral hemorrhages, most frequently subarachnoid haemorrhage from small arteries[1-4]. The incidence of MMD occurs in two peaks: the highest one during the first decade of life, and the lower one in the third decade[3,4,7]. Even in Japan, the incidence is estimated to be less than 1 in 100,000, more commonly described in females[3]. In Brazil, the incidence is not known; the first description in 1981 was by Minguetti and Ferreira[8] in a 3 year-old Japanese girl that developed multiple areas of cerebral infarction. In 1997, Minelli et al.[9] reported seven children and adults with MMD - cerebral infarction in five (75%) and intracerebral haemorrhage in two (25%). The age varied from eight to 45 years-old and 83% had motor and/or language disabilities that remained.

We report herein three cases of MMD in Brazilian (non-Japanese) young men with cerebral infarcts - a non-usual form of this disease according to reports from other countries[1-4].

METHOD

From 2378 cases with diagnosis of cerebrovascular disease registered from 1992 to 1996 (all patients aged 14 or more) in the Department of Neurology, Universidade Federal de São Paulo (UNIFESP) - Escola Paulista de Medicina (EPM), three cases had MMD according to the Suzuki and Takaku's angiographic classification (conventional angiography) and diagnostic guidelines for MMD proposed by the Ministry of Health and Welfare of Japan (MHWJ)[5,10] (Tables 1 and 2). Figures 1, 2 and 3 illustrate findings.

All patients were investigated through a standard screen for young stroke patients (SSYSP) including echocardiography, electrocardiography, chest radiography, tests for thrombophilia, autoantibodies and circulanting lupus anticoagulant, and cardiovascular examination. SSYSP and cardiovascular examination were normal in all patients, except in Patient 2 that had hyperlipidemia.

REPORT OF CASES

Patient 1. ARS, a 33 year-old melanodermic man presented two years previosly sudden numbness affecting his left side of face and left arm while working. Three days later he developed

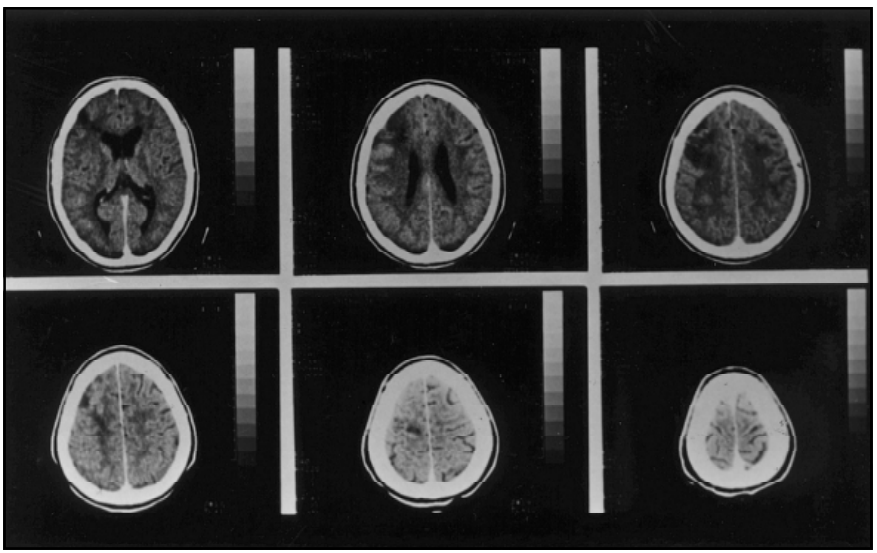

Fig 1. Contrast enhanced CT scan showing bilateral infarctions on MCA territory.

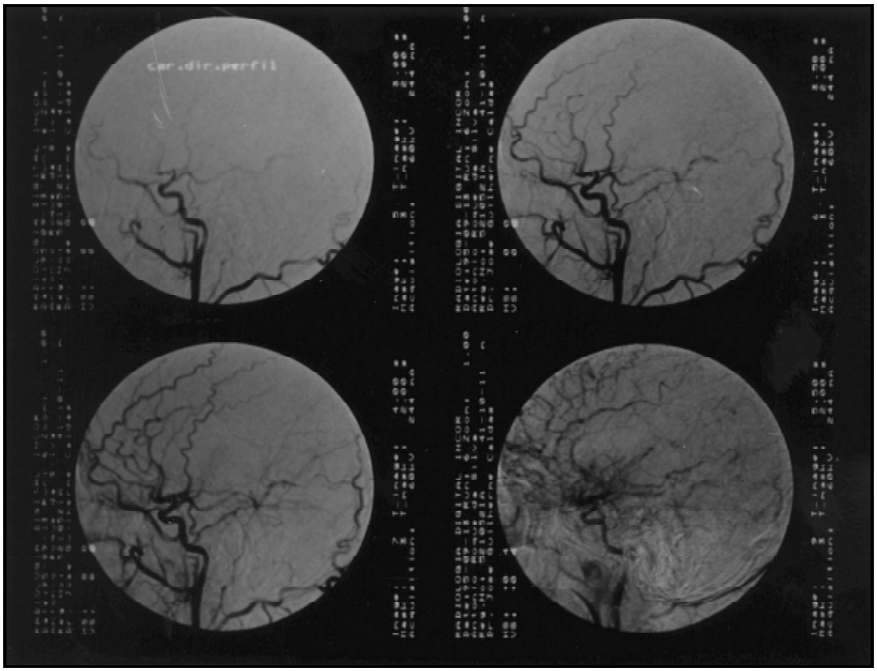

Fig 2. Intra-arterial angiography of the right ICA showing a stenosis with occlusion of the right MCA and stenosis of the right ACA.

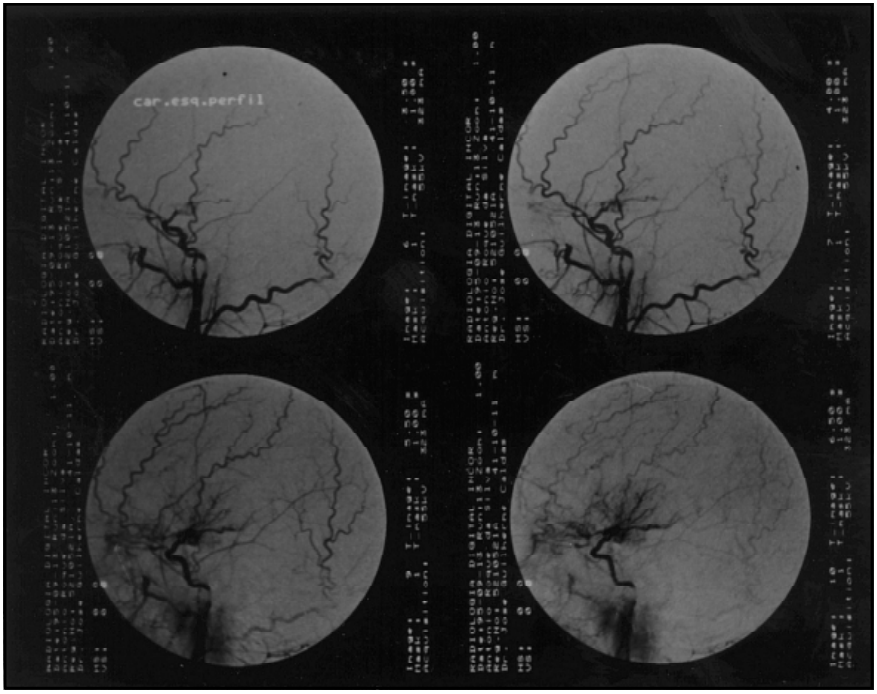

Fig 3. Intra-arterial angiography of the left ICA showing severe stenosis with occlusion of the left ICA and parenchymal collateral supply by moyamoya vessels and leptomeningeal collateral vessels.

Table 1. Angiographic classification (according to Suzuki and Takaku (1969).

Stage 1. stenosis of the carotid artery at its suprasellar portion, usually bilateral.
Stage 2. moyamoya vessels begin to develop at the base of the brain.
Stage 3. moyamoya vessels become more prominent as major trunks in the anterior circulation become severely stenotic or occluded.
Stage 4. posterior cerebral arteries are occluded, moyamoya vessels begin to diminish and collateral pathways from extracranial circulation develop.
Stage 5. moyamoya vessels are diminishing and extracranial circulation progresses.
Stage 6. moyamoya vessels and the major cerebral arteries completely disappear, the cerebral hemispheres receive blood through the abnormal extracranial-intracranial anastomosis.

Table 2. Diagnostic guidelines for MMD according to MHWJ.

1. Stenosis or occlusion of the intracranial internal carotid artery or the adjacent anterior and middle cerebral arteries.
2. Abnormal vascular network adjacent to the stenosed artery identified during the arterial phase of angiography.
3. Bilateral findings on angiography.
4. No other identifiable cause.

progressive left-sided weakness. He had smoked from the age of 19. Essential systemic arterial hypertension was detected 2 years before the event. Upon examination he had hemiparesis, spasticity and left sided hyperreflexia, and unmotivated laughter at tactile stimulation on paretic side. Contrast enhanced computed tomography (CT) showed bilateral infarcts on the MCA territory, larger at right. Magnetic resonance imaging (MRI) confirmed the extensive right sided infarct on the MCA territory, a smaller one on the left MCA territory, and a small infarct on the right anterior cerebral artery (ACA)territory. Intra-arterial digital subtraction cerebral angiography showed a stenosis of the right ACA and occlusion of the right MCA, severe stenosis with distal occlusion of the left ICA, and parenchymal collateral supply by MV and leptomeningeal collateral vessels. Findings were classified as Suzuki and Takaku's stage three on the right and stage two on the left. A cerebro-meningeal biopsy showed ischemic necrosis in organization without vasculitis. He was given aspirin - 300 mg once a day. He reported permanent left hemiparesis, unmotivated laughter disappearance and no additional symptoms during a one year follow-up.

Patient 2. JRF, a 32 year-old Caucasian man on April/1994 developed sudden unconsciousness with right-sided weakness. He had drinked heavily from the age of 18 until seven hours before the event. He had essential systemic arterial hypertension. Upon examination he showed expression aphasia, right hemiparesis with hypotonia and hyporeflexia. CT showed an infarct on the left MCA territory. MRI was not performed. Intra-arterial conventional cerebral angiography showed occlusion of the left ICA at the supraclinoidal portion and of the left MCA, with MV around. Suzuki and Takaku's classification: two/three on the left. A 300 mg dose of aspirin, to be taken once a day, was prescribed. In february/1995 he had two seizures and was given antiepileptic drugs with success. Upon review, he reported persistence of hemiparesis, improvement of speech disorder, and no new neurological symptoms during a follow-up period of two years.

Patient 3. RAM, a 14 year-old previously healthy Caucasian boy. In february/1992, during physical exercise, he developed a severe right-sided headache, speech disturbance and left- sided weakness. These symptoms disappeared hours later, but headache persisted. Eight days later he

awoke with speech disturbance and weakness on the left arm and leg. Upon examination he had a mild left hemiparesis and dysarthria. CT showed infarct in the bilateral MCA territory, which was more extensive on the right. Intra-arterial conventional cerebral angiography showed occlusion of the right ICA at the supraclinoid portion with MMV around and stenosis of the left intracranial ICA. Suzuki and Takaku's classification: stage two on the right and stage one on the left. He was not given any drug, yet his speech became normal and he had motor improvement on the right. No new neurological symptoms have been noted during a follow-up period of four years.

DISCUSSION

More than 40 years after MMD was recognized, it remains an intriguing illness. The etiology, natural history, pathogenesis and ideal treatment have been poorly defined[1,4,12,13]. This uncertainty is partly due to the absence of long-term follow-up[12]. There seems to be no relation to risk factors such as hypertension, diabetes or hyperlipidaemia[2]. We detected hypertension in two patients and hyperlipidemia in one, however we do not know if they are associated or co-existent conditions. Angiographic appearance of an abnormal vascular network at the base of the brain (moyamoya vessels) associated to identifiable cause is known as moyamoya syndrome[1,14,15].

The disease does not evidence arteritis, intimal thickening or medial thinning of the affected carotid arteries in histologic studies[2-4,7]. Bacterial infections have been associated with MMD[2]. Suzuki and Kodama in 1983 speculated that inflammation of the extensive sympathetic innervation of the ICAs may be responsible for these localized changes since there was clinical improvement with perivascular sympathectomy in some patients[2].

Typically, MMD starts in the first decade with complete stroke or recurring transient ischemic attacks -TIA- (sometimes induced by crying, coughing or straining) that cause motor, sensory, visual and speech disturbances, seizures, chorea and personality changes[1-4,12]. In adults, MMD is rare and 70 to 80% of patients develop bleeding in the basal ganglia, thalamus, or ventricles due to rupture of the fragile abnormal vessels. In non-Japanese adults MMD is rare, specially when presenting with cerebral infarction (described in 30 to 42% of the adults)[1]. Our patients were non-Japanese men aged 14 years or more that presented the "ischemic form" of MMD with TIA and/or infarctions in carotid territories. In Patient 3, the hyperventilation during exercise that caused precipitation of symptoms could represent critical perfusion in an area near infarction (right MCA territory).

CT and MRI can visualize intracranial changes in patients with MMD: multiple dilated abnormal vessels at the basal ganglia or thalamus (or both), narrowing or occlusion of major arteries of the circle of Willis, ischemic infarctions predominantly in watershed areas and hemorrhages[1,6,11]. In our patients, CT and/or MRI showed infarcts in the ACM territory in all and infarct in ACA territory in one, with centrum semiovale and basal ganglia affected in severe proportions. Infarctions in adults with MMD tend to occur in the watershed regions between anterior, middle, and posterior cerebral arteries circulation, mainly in the centrum semiovale and basal ganglia that are in a more vulnerable region supplied by long, penetrating branches of ACA and ACM. This might be explained by age-associated change in the capacity to form collateral pathways between basal perforating vessels and medullar arteries arising from ACA and ACM. Also, lenticulostriate arteries (some of the most important vessels among basal MV) become smaller in number and size with advancing age[1,2].

In a study of 518 patients reported by Nishimoto in 1979, the mortality rate was higher in adults (10%) than in children (4.3%), in whom the intracranial bleeding was the main cause of death[4].

Treatment remains unsatisfactory because the pathophysiology of MMD is still not unclarified. Conservative measures as vasodilators, steroids, anticoagulants and antibiotics have been used and considered ineffective[2,4]. However, cases with satisfactory follow-up, with non-surgical treatment were described, mostly in adults[3]. A surgical procedure for revascularization of the ischemic brain by creating collateral pathways has been considered the most reasonable treatment, especially for

children with ischemic symptoms. Surgical results including synangiosis, for which a muscle flap with its own established network of vessels is applied to the dural surface, and extracranial-intracranial bypass operations, for which isolated vessels are used, have showed a beneficial effect in some cases[2,4].

Our patients received conservative treatment. Two have taken 300 mg of aspirin a day, and their motor disabilities have improved without any deterioration over a follow-up period from one to four years. In Brazil, only 18 patients with MMD have been described up to 1997[9], but the disease may well be underdiagnosed.

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