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PROGRESSIVE CERVICOCRANIAL ARTERIOPATHY WITH DILATATIONS AND STENOSES

Case report

Adriana Bastos Conforto[1], Paulo Puglia Jr[2], Fábio Iuji Yamamoto[1], Milberto Scaff[3]

ABSTRACT - We report the case of a 36 year-old woman who presented occlusion of a basilar artery fusiform aneurysm (FA) associated with pontine infarction, and two episodes of subarachnoid hemorrhage possibly due to arterial dissection. She also had asymptomatic FAs in the right middle cerebral and left internal carotid arteries. Over 5 years, lesions suggestive of fibromuscular dysplasia in the right vertebral artery and occlusion of the left vertebral artery were observed. This combination of lesions emphasizes the possibility of a common pathogenetic mechanism causing different degrees of media disruption in cervicocranial arteries.

KEY WORDS: arterial cervicocranial disease, fusiform aneurysms, fibromuscular dysplasia, arterial dissection, subarachnoid hemorrhage.

Arteriopatia progressiva com dilatações e estenoses: relato de caso

RESUMO - Relatamos o caso de uma doente de 36 anos que apresentou oclusão de um aneurisma fusiforme de artéria basilar associado a infarto pontino e dois episódios de hemorragia subaracnóide provavelmente devido a dissecção arterial. Ela também apresentava aneurismas fusiformes assintomáticos na artéria cerebral média direita e na artéria carótida interna esquerda. Ao longo de 5 anos, lesões compatíveis com displasia fibromuscular foram observadas na artéria vertebral direita, assim como oclusão da artéria vertebral esquerda. Esta combinação de lesões sugere que um mecanismo etiopatogênico comum tenha causado diferentes graus de comprometimento da camada média de artérias cervicocranianas.

PALAVRAS-CHAVE: doença arterial cervicocraniana, aneurisma fusiforme, displasia fibromuscular, dissecção arterial, hemorragia meníngea.

The presence of dilatations in cervical or cranial arteries is a phenomenon that has received diverse and somewhat imprecise denominations, such as dilatative arteriopathy[1], arterial dysplasia[2], dolichoectasia[3] and fusiform aneurysms (FAs)[4-6]. The last two terms seem to designate different degrees of progression of the same disease. Etiopathogenic heterogeneity is suggested by descriptions of a number of wall abnormalities[1,6-11]. The most frequent findings in affected arteries have been loss of medial layer components, collagen fiber degeneration, fibrosis, atherosclerotic changes and parietal thrombosis[7,8,10,11]. FAs have been associated with trauma, infection, inflammation, atherosclerosis, arterial dissection or neoplasms[4]. However, in some cases no obvious predisposing factors or causes can be determined. FAs may be asymptomatic or cause brain stem and cranial nerve compression, subarachnoid hemorrhage (SAH) or infarction. The latter is more commonly caused by thrombosis of small collateral branches or embolism to distal arteries[3,9]. Complete occlusion of the affected vessel appears to be rare[12]. Association with stenotic lesions at other sites has been reported in fibromuscular dysplasia (FMD)[13-16].

We report the case of a patient whose distinctive features are the presence of FAs in the carotid and vertebrobasilar territories with both ischemic and hemorrhagic manifestations, left VA occlusion and development of FMD lesions in the right

Hospital das Clínicas/São Paulo University, São Paulo SP, Brazil (HC/FMUSP): [1]MD, Staff Neurologist, Neurology Department, HC/FMUSP São Paulo SP, (HC/FMUSP); [2]MD, PhD, Staff Neuroradiologist, Radiology Institute, HC/FMUSP; [3]Chief, Neurology Division, HC/FMUSP.

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Dra. Adriana Bastos Conforto - Departamento de Neurologia, Hospital das Clínicas/FMUSP - Avenida Dr. Enéas de Carvalho Aguiar 255 - 05403-000 São Paulo SP - Brasil. E-mail: abconf@usp.br.

VA. Clinical and neuroimaging follow-up findings, as well as possible mechanisms of pathogenesis are discussed.

CASE

The patient gave informed consent for the publication of this report. A 36 year-old woman was evaluated in our Neurology Department four days after presenting sudden, transient loss of consciousness followed by ataxia, deafness and tinnitus. One week before she had presented episodes of transient bilateral visual blurring. The neurological examination revealed vertical nystagmus, cerebellar ataxia, right anacusis, left hypacusis and right hemihypesthesia. Ten days after admission she presented right hemiparesis. Cranial computed tomography (CT) revealed a round, hyperdense structure situated anteriorly to the brain stem. The cerebrospinal fluid (CSF) contained 260 red cells and the protein concentration was 52 mg/dl. Magnetic resonance imaging (MRI) revealed a left pontine infarction. Transcranial Doppler suggested and digital subtraction angiography (DSA) confirmed a basilar artery (BA) occlusion (Fig 1). The diagnosis was thrombosis of a FA in the BA, associated with slight SAH. The latter might have been due to BA dissection, but angiographic signs of dissection were not present. The vertebral arteries (VAs) supplied both posterior inferior cerebellar arteries (PICAs). There were also very small FAs in the right middle cerebral artery (MCA) (Fig 2A) and supraclinoid portion of the left internal carotid artery (ICA) (Fig 2B). The patient did not have arterial hypertension. She had neither family history of known hereditary connective tissue disorders nor signs such as skin abnormalities, hyperextensible joints, marfanoid habitus, ectopia lentis or optic fundus abnormalities. Laboratory investigation was negative for systemic inflammatory and infectious disorders. Aspirin was prescribed, and the patient had progressive neurological improvement but did not completely recover.

Two months later, she presented sudden onset of headache, vomiting, dizziness and tinnitus. She had bilateral hypacusis, nystagmus and right hemiparesis. The CSF was xanthochromic and contained 2 white cells, 22 red cells and a protein concentration of 52 mg/dl. Two days later, the CSF had 595 red cells and a protein concentration of 70 mg/dl. An MRI was performed, disclosing hypersignal on the thrombosed portion of the BA, suggestive of a small bleeding. A second DSA was performed, and remained unchanged. Aspirin was maintained and the symptoms remained but gradually improved.

Three years later, a follow-up MRI showed only a single, old pontine infarction but magnetic resonance angiography (MRA) revealed signal changes suggestive of FMD, with a "string of beads" pattern in the right cervical VA. No flow signal was present in the proximal and middle portions of the BA, as well as in the intracranial right VA and throughout the left VA. The patient did not present new symptoms.

Five years later, the patient complained of spells of visual blurring, tinnitus and a burning sensation on the right eye, lasting for five minutes. The neurological examination revealed residual slight right arm weakness, right anacusis and left hypacusis. MRI disclosed an old pontine infarction. MRA revealed absence of signal in the left VA, right intracranial VA and BA. Signal changes in the right cervical VA, as demonstrated by the previous MRA, were still present. DSA disclosed BA occlusion and a "string of beads" pattern in the right cervical VA (Fig 3A). The right intracranial VA as well as the left extracranial VA were occluded (Fig 3B). FAs in the right MCA and left supraclinoid ICA were visible, as in the previous DSA. The CSF exam was normal. No aortic aneurysms were disclosed

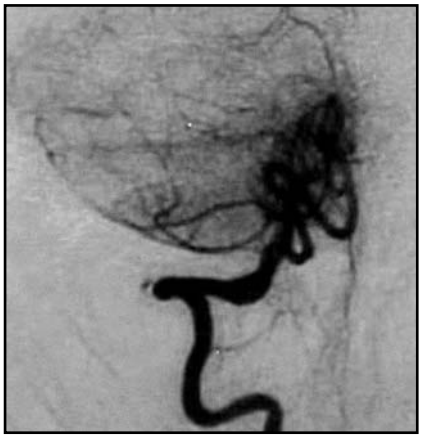

Fig 1. Right VA angiogram showing BA occlusion.

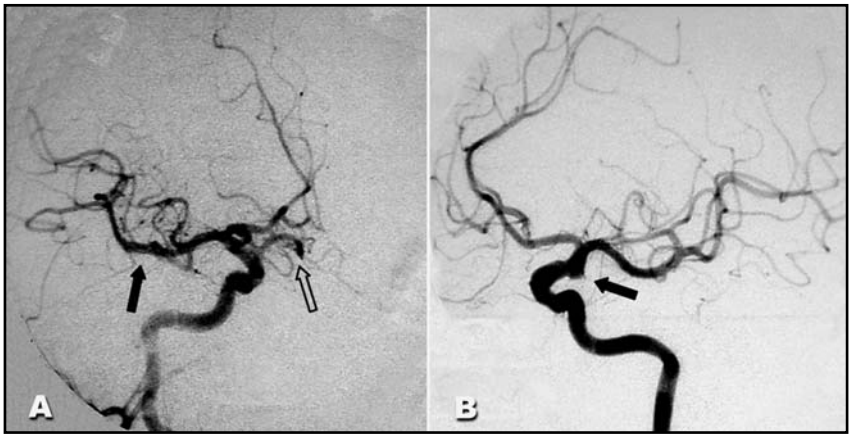

Fig 2. A) Right carotid angiogram showing a small FA (black arrow) in the right MCA. Dye goes from the right posterior communicating artery into the right posterior cerebral artery and rostral portion of the BA, distal to the BA occlusion (white arrow). B) Left carotid angiogram showing a small FA (arrow) in the supraclinoid portion of the left ICA.

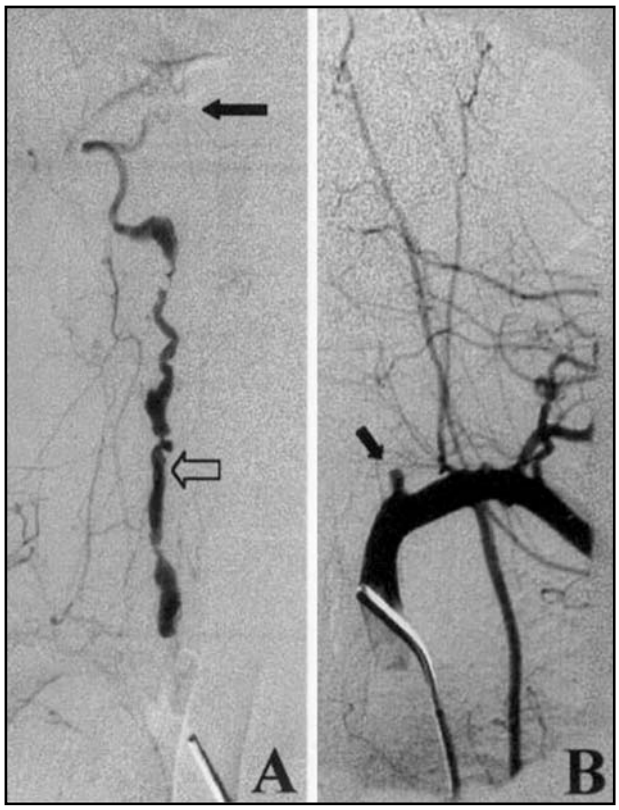

Fig 3. A. Right VA angiogram performed three years after onset of symptoms, showing BA occlusion, right intracranial VA occlusion (black arrow) and lesions characterized by a pattern of segmental dilatations and ring stenoses in the right cervical VA (white arrow), or "string of beads" type of FMD. B. Left subclavian angiogram showing left extracranial VA occlusion.

by transesophageal echocardiogram. Thoracic and abdominal CT did not reveal abnormalities in the aorta or other arteries. The patient was discharged on aspirin and clopidogrel, and remained asymptomatic.

DISCUSSION

Arterial cervicocranial disease coursing with dilatations is a rare and heterogeneous condition and FAs may be part of a spectrum of lesions within this condition. In a series of 85 patients, FAs and dissecting aneurysms were classified according to clinical presentation, characteristics of the internal elastic lamina (IEL), angiographic features and intraoperative appearance[8] as: classic dissecting aneurysm (type 1), segmental ectasia (type 2), dolichoectatic dissecting aneurysm (type 3) and saccular aneurysm, arising from arterial wall (type 4). Our patient would have, according to these criteria, a dolichoectatic dissecting basilar artery aneurysm (type 3) that bled and eventually underwent thrombosis, and also anterior circulation type 2 dilatations. The coexistence of these two types of dilatations in the same patient indicates the possibility of a common etiopathogenic process underlying both lesions.

It has been proposed that enlarging FAs would be more often related to non-atherosclerotic mechanisms associated with IEL or media weakness, while atherosclerotic processes would play a role in asymptomatic lesions that have a stable course[7]. Damage to the IEL and to the intima may be crucial to the pathogenesis of FAs since these components are extremely important to vessel strength[4-7,11]. Observations in animals and humans support this hypothesis. Injection of elastase into the media of the carotid artery has been associated with development of dilatations and elongations of the injected vessels in rabbits[17]. Miscellaneous conditions linked with arterial media involvement have been diagnosed in association with dilatative arteriopathy: FMD[13,14,16,18], giant cell arteritis[19], Anderson-Fabry disease[20], von Recklinghausen's disease[21], alpha-glucosidase deficiency[22], alpha-1 antitrypsin deficiency[23], and connective tissue disorders such as Marfan's syndrome[18,24]. Mechanical instability and loss of elasticity might predispose to dissection or distention at points of minor resistance in the arteries of affected patients.

It has been hypothesized that FAs may evolve from acute forms of dissecting aneurysms[7,25], but angiographic features are often non-specific. Intracranial artery dissection is a known cause of SAH. The patient had two episodes of slight SAH, the first in association with BA occlusion and pontine infarction. Therefore, dissection as well as aneurysm thrombosis are likely to have occurred.

The patient did not have risk factors for atherosclerosis and DSAs did not reveal abnormalities suggestive of diffuse atherosclerosis. However, follow-up over a period of five years revealed contiguous segments of dilatation and focal stenosis in the right VA. Such lesions have been described in FMD and other syndromic arterial lesions[2,13-16,18]. FMD is a nonatheromatous and noninflammatory angiopathy, more common in young females. The renal arteries are the most commonly affected vessels, followed by cephalic arteries. The extracranial ICAs are the most frequently affected cephalic arteries[14,26] while involvement of the VAs by FMD has been less frequently reported[10,15,27]. The "string and beads" angiographic pattern of FMD has often been histologically associated with medial fibroplasia, proliferation of fibrous tissue or col-

lagen as well as with microaneurysms in the media layer[14]. Arterial dissections may occur as complications of FMD[14] and are likely to be related to vessel wall frailty. Coexistence of FMD and connective tissue disorders has been reported and it has been suggested that FMD might be a nonspecific manifestation of such disorders[18]. The patient did not have signs of connective tissue disease but this diagnosis could not be completely ruled out. Ultrastructural connective tissue abnormalities have been described in skin biopsies of patients with cervical artery dissections who had no other clinical manifestation of a connective tissue disease[28], alerting to phenotypical heterogeneity.

The association between FMD and intracranial saccular aneurysms or FAs has also been established[13,14,16]. Increase in FA size and "de novo" FAs have been described in the literature, in association or not with FMD[7,26,29].

In conclusion, in the present case angiography disclosed FMD lesions on the right VA, occlusion of the left extracranial and right intracranial VAs, as well as occlusion of a BA aneurysm, possibly associated with dissection. In addition, she also had two asymptomatic FAs in the right MCA and left ICA, in the absence of contiguous FMD angiographic lesions. The presence of this peculiar combination of lesions in a single patient points to a common pathogenetic mechanism affecting the arterial media layer, presenting with a continuum of manifestations ranging from FMD lesions to FAs in anterior and posterior intracranial arterial territories.

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