Bilateral steno-occlusive disease of the middle cerebral artery: a case report with clinical-hemodynamic mismatch

Helena Rocha¹, Pedro Castro¹, Rosa Santos¹, Elsa Azevedo¹, and Marta Carvalho¹

Abstract

Background: Bilateral steno-occlusive disease of middle cerebral artery (MCA) in young adults raises significant issues regarding etiology and treatment. The potential concomitance of hypoperfusion in the affected territories is of particular clinical relevance.

Case report: A 37-year-old man was admitted for a right MCA transient ischaemic attack. He was smoker, obese, dyslipidaemic, with previous history of heroin addiction and cured B and C hepatitis virus infections. Brain magnetic resonance and cardiac evaluation were normal. Transcranial color-coded sonography (TCCS) showed >50% proximal right MCA stenosis and distal left MCA occlusion. Treatment with aspirin and statin was started. Three months later, TCCS revealed >70% right MCA stenosis and left MCA occlusion. Selective angiography confirmed the steno-occlusive disease. Cerebrospinal fluid analysis revealed increased protein levels and a normal cell count. Corticotherapy was started, but the patient did not complied. Bilateral occlusion of MCA was noticed on TCCS, one month later, being the patient asymptomatic. Pulsed arterial spin labelling (PASL) revealed a severe decrease of cerebral blood flow in the distal part of both MCA territories.

Conclusions: The etiology of this progressive steno-occlusive disease remains unknown. Atherosclerosis may be a possible mechanism, however other potential etiologies must be considered giving the rapidly progressive character of the disorder. As it seems to be now stabilized, we wonder if it can be due to the vascular risk factors control and antithrombotic treatment or to a non-identified inflammatory monophasic cause. Serial TCCS played a major role in the assessment of disease progression.

Keywords: Progressive intracranial stenosis, Brain hypoperfusion, Transcranial color-coded sonography, Pulsed arterial spin labeling.
Introduction

Progressive bilateral steno-occlusive arteriopathy in young adults is rare and raises significant issues concerning etiology, treatment, and prognosis [1, 2]. Atherosclerotic disease can be a major cause, but other causes such as vasculitis or non-inflammatory arteriopathies are not to be dismissed [3, 4]. Imaging techniques are crucial for diagnosis and for follow-up, providing information about hemodynamic status and consequently about the risk of ischemia.

Case report

A 37-year-old Caucasian man was admitted to the emergency room for two transitory episodes of dysarthria and sensory disturbance in the left face and arm. He worked as a cargo driver and had 6 years of formal education. He was smoker, obese, binge drinker, and previously addicted to heroin until fourteen years ago. His father had a stroke at the age of fifty, and additional family history was irrelevant. Physical examination, including neurological assessment was unremarkable. Brain CT, blood routines, ECG and electroencephalography were normal. Since the symptoms were suggestive of transient ischemic attacks (TIA) he was started on aspirin and was admitted to the Neurology Department for further investigation.

An exhaustive analytical study was performed (Box 1) and revealed dyslipidemia and cured hepatitis B and C infections. Transcranial color-coded sonography (TCCS) revealed a pattern of thrombolysis in brain ischemia (TIBI) score of 4 in proximal right middle cerebral artery (MCA) and 3 in left MCA, suggesting respectively >50% stenosis and occlusion patterns (Figure 1a and 1b). Trans-esophageal echocardiogram was normal. Brain magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) did not show parenchymal lesions suggestive of acute or previous ischemia (Figure 2a). Three-dimensional time-of-flight magnetic resonance angiography (MRA) showed an absent flow signal in the left MCA and a severe stenosis in the proximal right MCA (Figure 2b). The patient was discharged on aspirin and statin.

Three months later, a routine TCCS revealed worsening right MCA stenosis (TIBI 4 but with velocity ratio to pre-stenosis >3, suggesting stenosis >70%) and persistence of left MCA occlusion (Figure 1c and 1d). At that time the patient had quit smoking and lipid profile was already normal. Selective digital subtraction angiography (DSA) showed a focal stenosis of 50% of the supraclinoid portion of the right internal carotid artery (ICA); irregular vessel wall of proximal right MCA causing a severe stenosis (65-70%) at this location; and left MCA occlusion with collateralization by pial branches of anterior cerebral artery (ACA) and external carotid artery (Figure 2d1 and 2d2). Cerebrospinal fluid (CSF) analysis revealed increased protein (1,00g/L), with a normal cell count (5cells/ul). Despite lack of any particular evidence of cerebral vasculitis, but due to its possibility, a pulse of methylprednisonone 1g/day IV was administered for 5 days.

One month later bilateral MCA TIBI 3 occlusion pattern was noticed on TCCS, although the patient remained asymptomatic (Figure 1e and 1f). Cerebral vasoreactivity was tested with apnea test in the visible segment of what could be M1 segment of MCA, or a local collateral vessel, showing lack of reactivity (Figure 3). Oral prednisolone 60mg was started, but the patient did not comply for more than one week due to fear of potential side effects. The pattern of brain perfusion was evaluated with pulsed arterial spin labeling (PASL) MRI, which confirmed a severe decrease of cerebral blood flow in the distal part of both MCA territories (Figure 2e).

One year after the presenting symptoms, cerebral DSA confirmed persistence of bilateral proximal MCA occlusions, with extensive collateralization from pial vessels from ipsilateral ACA, and mild right supraclinoid ICA stenosis (Figure 2d3 and 2d4). Other cerebral and supra-aortic branches were unremarkable. Abdominal DSA showed no vessel abnormalities in other arterial territories.

The patient remains asymptomatic, without focal neurological deficits, although a more comprehensive neuropsychological assessment suggested a cognitive impairment (The Montreal Cognitive Assessment - MoCA 22/30) with memory dysfunction.

Box 1. Analytical study performed in the Neurology Department (only the abnormal results are discriminated).

<table>
<thead>
<tr>
<th>Complete blood count</th>
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<tbody>
<tr>
<td><strong>Biochemical</strong></td>
</tr>
<tr>
<td>Glycaemia, protein, albumin</td>
</tr>
<tr>
<td>Serum electrolytes, Inflammatory markers (C-Reactive protein, Sedimentation rate)</td>
</tr>
<tr>
<td>Thyroid, liver, renal function, ADA, ECA</td>
</tr>
<tr>
<td>Lipid profile (Total cholesterol 246mg/dl, LDL 169mg/dl, HDL 38mg/dl and triglycerides 193mg/dl)</td>
</tr>
<tr>
<td><strong>Viral Serology</strong></td>
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<tr>
<td>Serum titers for syphilis and HIV negative; previous hepatitis B and C virus infections (AcHBc positive, AgHBs negative; AcHCV positive, RNA HCV negative)</td>
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<tr>
<td><strong>Immunology</strong></td>
</tr>
<tr>
<td>ANA, anti-dsDNA, anti-ENAs, complement, ANCA, lupus anticoagulant, anticardiolipin, anti-B2 glycoprotein antibodies</td>
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<tr>
<td><strong>Coagulation / Prothrombotic study</strong></td>
</tr>
<tr>
<td>aPTT, PT, AT III, Protein C and S, MTHFR, Factor V Leiden, prothrombin G20210A mutation, homocysteine (homozygous C677T MTHFR mutation)</td>
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</table>
Discussion

We report a case of bilateral progressive steno-occlusive disease of MCA in a 37-year-old man with multiple vascular risk factors, past history of illicit drugs consumption and markers of cured hepatitis B and C infections. The etiology remains unknown. Atherosclerosis may be a possible pathological mechanism in this case [3]. In fact, atherosclerotic stenosis of the major intracranial arteries may be the most common cause of stroke worldwide, although not in Caucasians. Patients with symptomatic severe intracranial stenosis (>70%) have a risk of recurrent stroke as high as 23% in 1 year [4-6]. In this particular case, the rapidly progressive character of the disease imposes the exclusion of other potential etiologies.

The prothrombotic study, performed as a routine in young adults, revealed normal homocystein level and homozygous C677T MTHFR mutation. The association between this genotype and cerebrovascular disease is still controversial although it has been previously reported as
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Figure 2. (a) Brain MRI with fluid attenuated inversion recovery (FLAIR) sequence: no parenchymal lesions; (b) Three-dimensional time-of-flight magnetic resonance angiography (MRA): absent flow signal in the left MCA and a severe stenosis in the proximal right MCA; (c) Pulsed arterial spin labeling (PASL): hypoperfusion in the distal part of both MCA territories; (d) Cerebral digital subtraction angiography (DSA): July 2012 – focal stenosis of 50% of the supraclinoid portion of the right ICA and irregular vessel wall with severe stenosis (65-70%) of proximal right MCA (d1), left MCA occlusion with collateralization due to pial branches of anterior cerebral artery (ACA) and external carotid artery branches (d2); One year later – proximal right (d3) and left MCA occlusions and left internal carotid artery (ICA) stenosis in the supraclinoid portion (d4) with exuberant collateralization.

In our workup, the non-specific CSF findings, the normality of brain parenchymal MRI and the absence of irregularities such as beading or focal narrowing of brain vessels on DSA do not favor this diagnosis [10-13]. Even though, treatment with corticotherapy was tried, its effectiveness could not be evaluated because of patient’s non-compliance. The angiographic collateralization pattern has some similarities with moyamoya vessels, which typically develop in cases of progressive stenosis of the terminal portion of the ICA and its main branches (ACA and MCA) [13-15]. Although the patient might have a moyamoya syndrome, the Moyamoya disease, which occurs typically in Asian people, is not a likely diagnosis [16, 17].

In what concerns heroin consumption, most strokes attributed to this drug occur acutely after its administration, mainly due to global brain hypoperfusion or cardio-
embolism, because of infective endocarditis. A few reports also suggest an underlying vasculitic process but this is not widely accepted once there is no pathological proof [18, 19]. There is no evidence of recent consumptions in this patient.

We emphasize the usefulness of serial TCCS in the diagnosis and follow-up of intracranial stenosis. Being the patient asymptomatic and having a brain MRI without abnormalities, the routine evaluations with this non-invasive technique were crucial to assess disease progression [20–22]. Brain perfusion pattern was also evaluated using a non-invasive MRI method—PASL, that uses magnetically labeled water protons as an endogenous tracer [23–26], which revealed bilateral cerebral hypoperfusion. This was discrepant with the absence of focal signs, although it might explain the cognitive disturbance.

Apart from the rapid progression of the intracranial stenosis at first, the process seems to be now stabilized, as the patient remains asymptomatic and no other vessels abnormalities were detected. We wonder if this stability can be assigned to the vascular risk factors control and antithrombotic treatment effect or if there was a non-identified inflammatory monophasic cause. As mentioned, establishing an etiology remains a challenge.

Competing interests
The authors declare no conflict of interest.

References

Abbreviations
ACA: Anterior cerebral artery; CSF: Cerebrospinal fluid; DSA: Digital subtraction angiography; DWI: Diffusion-weighted imaging; ICA: Internal carotid artery; MCA: Middle cerebral artery; MRA: Magnetic resonance angiography; MRI: Magnetic resonance imaging; PASL: Pulsed arterial spin labeling; TCCS: Transcranial color-coded sonography; TIA: Transient ischaemic attacks

Figure 3. Apnea test: Cerebral blood flow velocity (cm/s) at middle cerebral artery (MCA) level was monitored with transcranial Doppler bilaterally (right, blue; left, red). Apnea was performed for 22 seconds (grey box). Note that cerebral blood flow waveforms remained unchanged during hypercapnia. Low Breath hold indexes (right -0.22; left 0.46) were calculated, confirming low cerebrovascular reactivity (normal values: 1.2 ± 0.6) [27].
27. Markus HS, Harrison MJ. Estimation of cerebrovascular reactivity using transcranial Doppler, including the use of breath-holding as the vasodilatory stimulus. Stroke 1992; 23:668-673