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Radiological findings of a symptomatic carotid pseudocclusion: ''Guadiana river sign''☆,☆☆

Hallazgos radiológicos de una pseudooclusión carotídea sintomática: signo del Guadiana

Dear Editor,

> ''Your squire Guadiana, lamenting your hard fate, was in like manner metamorphosed into a river that bears his name; yet still so sensible of your disaster, that when he first arose out of the ground, to flow along its surface, and saw the sun in a strange hemisphere, he plunged again into the bowels of the earth; but the natural current forcing a passage up again, he reappears again and again...''[1]
>
> Miguel de Cervantes Saavedra

Pseudocclusion of the internal carotid artery (ICA) is the consequence of a large atheromatous lesion causing high-degree stenosis. This lesion is commonly located in the proximal segment of the ICA or at the level of the carotid bifurcation, giving rise to a filiform flow in the distal portion followed by recovery of its normal lumen.[2]

In 1967, Davies and Sutton were the first to refer to a slowing of the carotid flow in the context of their study of intracranial hypertension.[3] Lippman et al.[4] described an atherosclerotic lesion in the ICA and distinguished it from carotid hypoplasia.

Pseudocclusions may result from carotid dissection, whether traumatic or spontaneous, or else from stenosis secondary to a radiation-induced arteritis, congenital carotid hypoplasia, or a severe diffuse atheromatous lesion extending distally[5] and mimicking a complete occlusion. This erroneous impression frequently arises when the working diagnosis has been determined using a single non-invasive imaging technique which does not enable reliable identification of a critical stenosis or pseudocclusion of the ICA. Combining several non-invasive techniques to study an apparent occlusion increases their diagnostic ability considerably, with no need for such invasive techniques as angiography. However, radiological findings characteristic of a carotid pseudocclusion have classically been defined by angiography, and they are traditionally grouped under the term 'carotid string sign'.

Carotid string sign

The radiological terms 'carotid slim sign' or 'carotid string sign' refer to the angiographic finding of a critical stenosis of approximately 99%, located at the root of the ICA, with preserved patency of the threadlike distal segment.[2]

Many diverse and different findings have been included under the umbrella term 'string sign': from carotid artery disease (mentioned above) to the narrowing, frayed appearance of the terminal ileum in the context of inflammatory bowel disease. In neurology, and especially in the field of stroke, the term 'string sign' is usually associated with a hyperdense artery during ischaemic stroke in the hyperacute stage. Even so, questions remain about the validity of using a catch-all heading under which such different diseases are included.

Guadiana river

The seeming disappearance and distal reappearance of blood flow, which are characteristic of carotid pseudooclusion, are reminiscent of the 'hidden' course of the Guadiana river, the Iberian peninsula's fourth greatest river in terms of length and discharge. It runs east to west from Castille-La Mancha across Andalusia to reach Extremadura, where it finally turns south to mark the Spanish-Portuguese border before flowing into the Atlantic Ocean. The course of the river disappears in the vicinity of the town of Argamasilla de Alba (Castille-La Mancha) to later reappear through natural apertures, such as those located near Villarrubia de los Ojos, gateway to the springs known as the ''Ojos del Guadiana''. The river's underground course is explained by the multiple cracks in the rocks which enable the water to flow through an aquifer system before reaching the surface again.[6]

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Clinical case

To illustrate the Guadiana river sign, we present the case of a 64-year old man who awakened suddenly with a severe headache irradiating to the right cervical region, followed by dysarthria and transient left-side weakness which was predominantly faciobrachial. Symptoms resolved within an hour. His medical history included arterial hypertension and smoking until the age of 40. The cranial CT scan yielded normal results, as did the routine blood test, the electrocardiogram, and the echocardiogram.

The carotid Doppler ultrasound revealed an apparent distal occlusion of the ICA, with no signs of dissection, contrary to our initial clinical suspicion. Diffusion-weighted magnetic resonance imaging (MRI) showed punctiform ischaemic foci in the right cerebral hemisphere at the prefrontal, temporoparietal, and parieto-occipital levels. The MR angiography (MRA) of the neck showed an occlusion of the right ICA at the level of the carotid sinus, 5 mm from its root, with absence of flow at the base of the skull. We also observed that the diameter of the external carotid artery was comparatively larger, but no signs of dissection were seen on time-of-flight sequences. The intracranial MRA showed a pattern characteristic of collateral circulation in the context of an apparent occlusion of the right ICA. This circulation passed through the anterior communicating artery, with antidromic flow of the anterior cerebral artery filling the middle cerebral artery, which appears attenuated; collateral circulation is lacking in the right posterior cerebral artery (Fig. 1 A and B). Sequential CT angiography showed high-degree stenosis of the ICA with the seeming disappearance and subsequent reappearance of blood flow. It also revealed the presence of critical stenosis >99% affecting the distal portion of the carotid sinus. Stenosis was associated with a calcified atherosclerotic plaque; the intraluminal filling defect disappeared and flow was observed at the level of the cavernous sinus (Fig. 2).

After the initial cranial CT scan, the patient received triple antiplatelet therapy as a participant in a clinical trial comparing triple therapy to standard antiplatelet therapy for secondary prevention of minor ischaemic stroke and high-risk transient ischaemic attacks. In view of these findings, a right thromboendarterectomy was performed at 30 days. The patient remains asymptomatic to date, and his treatment consists exclusively of clopidogrel 75 mg, atorvastatin 40 mg, and quinapril 5 mg.

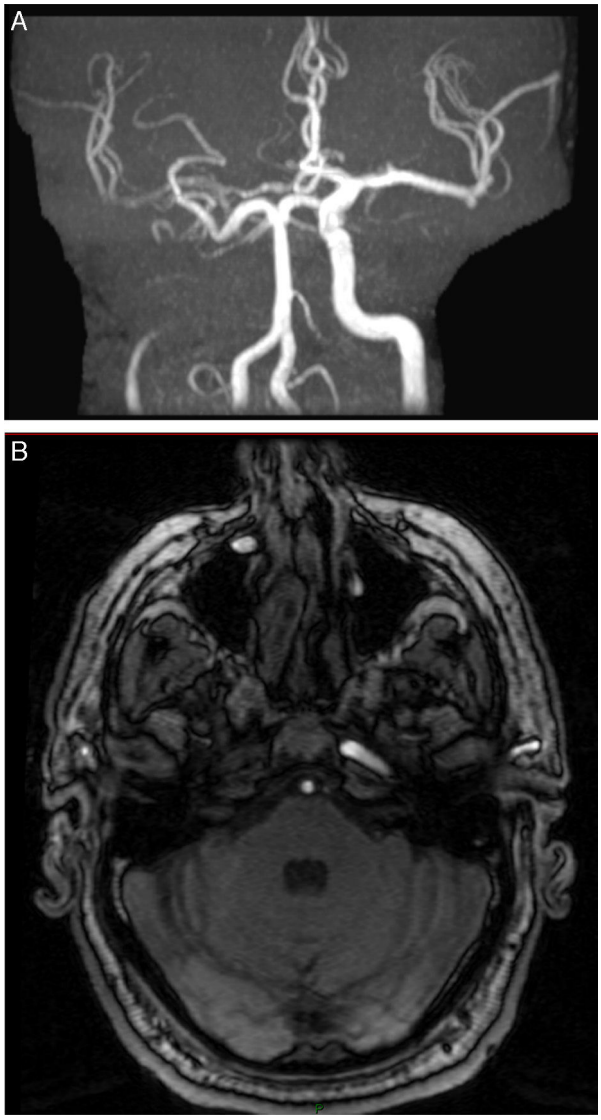

Figure 1 (A, B) Nuclear MRA shows an apparent occlusion of the right internal carotid artery at the level of the carotid sinus 5 mm from its root and absence of flow at the base of the skull. The images show a collateral circulation pattern passing through the right anterior communicating artery, with antidromic flow in the anterior cerebral artery filling the ipsilateral middle cerebral artery, which appears attenuated. Collateral circulation is absent in the right posterior cerebral artery.

Discussion

The NASCET criteria for measuring carotid stenosis tend to underestimate the degree of severity of pseudocclusions since the diameter of the ICA decreases as the degree of obstruction increases. Therefore, some authors have proposed using exclusively angiographic and qualitative criteria to identify pseudocclusion of the ICA.[7] These criteria include: an ICA with a diameter smaller than that of the external carotid; opacification in the distal territory of the ICA, which again would be smaller than the external carotid; and compensation by means of collateral intracranial circulation.[8]

Collapse of the distal ICA caused by atherosclerotic plaque, observed during surgical examination of the neck, represents the main feature in carotid pseudocclusion; the treatment of choice is thromboendarterectomy.[9] Despite the important advances in such non-invasive imaging techniques as Doppler ultrasound, MRA, and CT angiography, conventional angiography or arteriography is still considered the most accurate diagnostic method or gold standard with which to examine this phenomenon. However, newly-developed non-invasive techniques provide sufficiently valid information, especially when used in combination, to let us distinguish between complete occlusion and pseudocclusion

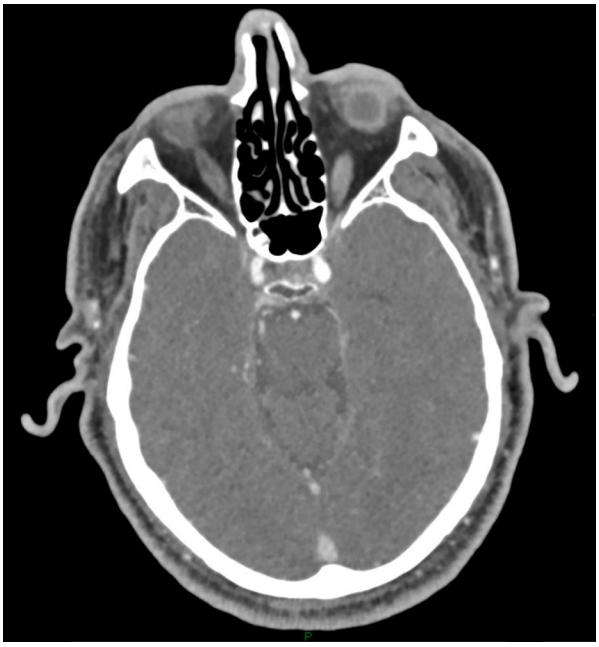

Figure 2 Angio-CT shows flow in the right internal carotid artery at the level of the cavernous sinus. Flow had disappeared at the level of the base of the skull.

in clinical practice without any need for more invasive methods.

Nevertheless, usefulness of conventional angiography in specific cases should not be underestimated. Portuguese neurosurgeon António Egas Moniz (1874—1955) developed the 'arterial encephalography' method which resulted in several well-known clinical applications. He was awarded the Nobel Prize in Physiology or Medicine not for that innovation, but rather for his pioneering studies of psychosurgery in which he treated psychosis with prefrontal leucotomy. The latter technique was later optimised and polished when he returned to the Iberian Peninsula to work with the great Basque neurosurgeon Juan Burzaco Santurtún (1930—2006). In 1928, Ferrán Martorell became the first doctor in Spain to perform an angiography following Egas Moniz's method.[10]

The use of angiography over the years continues in the procedures routinely employed in current practice: for example, thrombolysis during the acute phase of ischaemic stroke or angioplasty as an interventional therapeutic alternative to thromboendarterectomy. Among non-interventional radiology techniques, MRA and time-of-flight sequences alone are not currently able to calculate the minimum residual flow precisely enough to identify presence of critical stenosis, that is, presence of a carotid pseudocclusion treatable by surgery. However, these techniques are more reliable when combined with each other or with other techniques.[11,12]

Guadiana river sign

Currently, there is no consensus on the term used to refer to pseudocclusion of the ICA, an entity also known as subocclusion, preocclusion, or critical stenosis. The most widely accepted term is 'string sign', despite the multiple meanings that we mentioned previously. We believe that the concept of a river whose course disappears and later reappears, similarly to what occurs in carotid pseudocclusion, is more explanatory. With the above in mind, and considering the waning use of conventional angiography studies for presurgical evaluation of ICA and the frequent references to a 'string sign' in other fields of vascular neurology or medicine, we suggest 'Guadiana river sign' as a term for carotid pseudocclusion.

The Guadiana river, whose underground course was described by Cervantes, is a metaphor evoking the seeming disappearance and subsequent reappearance of vascular flow that characterises a carotid pseudocclusion. A sign by this name pays tribute to *Don Quixote*, that masterpiece of universal literature whose second part recently celebrated its four hundredth year.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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Progressive multifocal leukoencephalopathy in an immunocompetent patient☆

Leucoencefalopatía multifocal progresiva en un paciente inmunocompetente

Dear Editor,

Progressive multifocal leukoencephalopathy (PML) is a condition caused by reactivation of the JC virus (JCV) in severely immunodeficient patients, for example, HIV-infected patients or patients treated with immunosuppressants. It affects oligodendrocytes in the central nervous system, causing such neurological symptoms as epileptic seizures, behaviour disorders, motor impairment, and ataxia. Symptoms are progressive. Typical neuroimaging findings include multifocal lesions in subcortical areas, normally with no mass effect or contrast uptake.

Diagnosis is based on clinical or radiological suspicion of the disease combined with detection of JCV DNA in CSF by PCR testing. Definitive diagnosis is reached when JCV DNA or viral proteins are detected in brain tissues. Treatment of immunodeficient patients with PML aims to restore immune system function by either administering antiretroviral treatment or discontinuing immunosuppressive drugs.

However, PML may also affect immunocompetent individuals.

We present the case of a 72-year-old man with no relevant medical history who visited the emergency department due to progressive gait impairment and a 5-month history of visual field alterations.

The physical examination revealed left-sided visual extinction and moderate weakness of the left lower limb. Neuropsychological tests confirmed visual extinction and revealed dyslexia, acalculia, and dysgraphia.

An MRI scan revealed hyperintensities in the right parieto-occipital area as well as in the subcortical area in T2/FLAIR sequences; no contrast uptake or mass effect were seen. The area appeared bright in diffusion-weighted images and no ADC restriction was observed. A spectroscopy study displayed a slight increase in the Cho/NAA ratio and presence of lipids and lactate.

All these findings suggested an infectious or inflammatory aetiology, with neoplasia being less likely. A thorough blood analysis revealed normal results for vitamins, thyroid hormones, and tumour markers, and no HIV infection. The results of a white blood cell count and peripheral blood smear also yielded normal results. A thoracic-abdominal CT scan revealed no signs of neoplasia.

As the patient remained stable and MRI findings were non-specific, we scheduled an additional MRI scan to be performed a few weeks later. However, 2 weeks after discharge, the patient returned to the emergency department due to clinical deterioration, left hemiparesis, and aphasia. An additional MRI scan revealed that the affected area had increased and now extended to the cortical area and corpus callosum (Fig. 1). In light of a suspected inflammatory or infectious process, we decided to perform a lumbar puncture. The CSF analysis revealed slightly increased protein levels (62.2 mg/dL; 5 leukocytes/mm^3, 110 erythrocytes/mm^3, glucose 72 mg/dL), and no oligoclonal bands.

Since both symptoms and the lesion were progressing rapidly, we decided to conduct a brain biopsy, which revealed atypical nuclear inclusions in astrocytes, with proliferation and accumulation of foamy macrophages. An immunohistochemical study showed p53 overexpression and increased expression of SV40 (polyomavirus large T antigen) in astrocytes, as well as viral inclusions displayed by electron microscopy (Fig. 2). These findings were compatible with definitive diagnosis of PML. The PCR study of JCV in CSF yielded 50 536 copies/mL.

Our patient died a month after diagnosis due to disease progression.

PML is extremely rare in immunocompetent patients. Only 7 cases have been described to date; of these, only 4 were confirmed histologically.[1—6] In some of these cases, it was unclear whether immune system imbalances were present. For example, one patient had low levels of IgA, CD8, and natural killer cells; another patient had a hepatitis B infection; and another patient had type 2 diabetes mellitus and low levels of IgG and IgM, and had not been tested for

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