Neurological Sciences (2019) 40:635–637
https://doi.org/10.1007/s10072-018-3615-8

LETTER TO THE EDITOR

Moyamoya masquerading as relapsing remitting multiple sclerosis

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Received: 2 July 2018 / Accepted: 18 October 2018 / Published online: 27 October 2018

Dear Dr. Federico,

Despite evolving diagnostic criteria and improved imaging techniques, multiple sclerosis (MS) is often misdiagnosed [1, 2]. Many neurological conditions may mimic MS [3], making careful examination of clinical history, paraclinical results, and imaging findings extremely important when considering differential diagnoses for neurological symptoms. In this report, we present the case of a woman diagnosed with MS who was found instead to have Moyamoya disease (MMD). MMD is a cerebral angiopathy that presents with specific radiological manifestations, as well as symptoms consistent with transient ischemic attacks (TIAs)/strokes [4, 5]. When crafting a differential diagnosis for MS, clinicians should remain cognizant of the radiological and clinical manifestations of MMD and other vascular neurological syndromes.

A 44-year-old, Caucasian, left-handed female presented to our MS center for advice regarding MS management. Her neurological symptoms began during her teenage years during which she would experience one to two headaches per week. These headaches lasted a few hours each and included tightness, pressure, and a band-like pain (4/10 severity) that affected primarily the biparietal and bitemporal regions, with occasional involvement of bilateral frontal areas. Over time, the headaches evolved to last days and were accompanied by severe photophobia and nausea, characteristic of migraines. In her twenties, the patient experienced three episodes of abrupt-onset left-sided facial and tongue numbness lasting 2–3 h that resolved spontaneously. She also experienced episodic dizziness and lightheadedness 2–3 times per week, as well as persistent fatigue.

Following an episode of self-limiting, sudden-onset, left foot dragging, she underwent an MRI of the brain. This demonstrated non-specific white matter lesions (Fig. 1a, b). Subsequently, she underwent a lumbar puncture, which demonstrated routine cerebrospinal fluid (CSF) constituents within normal limits, as well as negative oligoclonal bands and normal IgG index. Despite the transient nature and abrupt onset of neurological symptoms, and the nondescript white matter changes on MRI, she was considered to have possible MS and was commenced on treatment with interferon beta-1b. Thereafter, she subjectively felt that her headaches, dizziness, lightheadedness, and fatigue transiently improved for a number of months, but then ultimately returned.

Prior to our assessment, the patient experienced two episodes of abrupt-onset, transient, expressive dysphasia. The patient reported that there was consideration for changing her MS therapy, which prompted a referral to our center. Neurological examination demonstrated left lower extremity hyperreflexia. Otherwise, her examination was unremarkable. MRI and CTA of the head, and cerebral angiogram are illustrated in Fig. 1.

Collating the history of abrupt-onset neurological episodes, unremarkable CSF, and multi-modal imaging findings, MMD was diagnosed. The patient's episodes of left-sided weakness and numbness were likely caused by hypoperfusion due to Moyamoya changes and decreased flow within the right middle cerebral artery. Similarly, cerebral hypoperfusion was also the likely cause of the intermittent episodes of lightheadedness and dizziness. With respect to the two episodes of expressive dysphasia, given that the patient was left handed, it is possible that her speech centers may have been right hemisphere dominant. Finally, cortical irritability due to chronic hypoperfusion may have contributed to the headaches and migraines. Upon diagnosis with MMD, the MS treatment was discontinued and aspirin commenced. The patient remains event-free 2 years later.

This case highlights the importance of thoroughly examining patient history and radiological findings in the work-up of suspected MS. In this case, the patient's neurologic history was not consistent with MS. While migraines may occur in patients with MS, they are unlikely to reflect disease activity [6]. Contrarily, migraine-like headaches occur in up to two thirds of Caucasian patients with MMD [4, 7]. Additionally, while numbness and weakness often occur in patients with MS, these symptoms typically persist for greater than 24 h.

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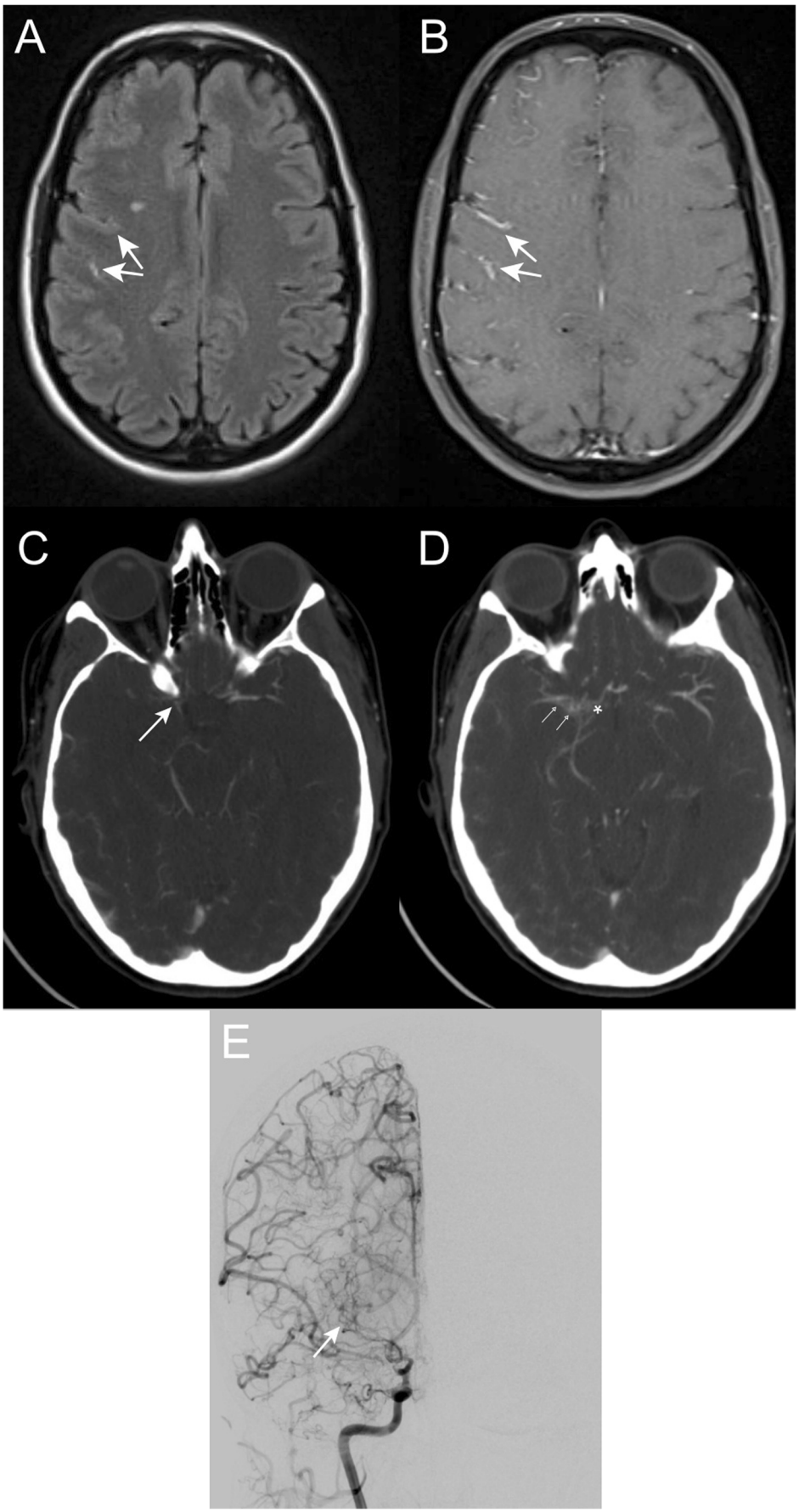

Fig. 1 Evidence of Moyamoya disease on brain MRI, head CTA, and cerebral angiogram. *MRI brain*. Axial fluid-attenuated inversion recovery (FLAIR) sequences demonstrate non-specific right frontal white matter hyperintensities (**a**). High signal intensity is demonstrated along the leptomeninges of the right cerebral convexity (arrows), which is further appreciated on gadolinium-enhanced T1 sequences (**b**, arrows; ivy sign). *Head CTA.* This demonstrates marked narrowing of the right terminal internal carotid artery (ICA) and M1 origin (**c**). **d** Tiny vessels are visualized near the narrowed distal right ICA (asterisk symbol), compatible with hypertrophied lenticulostriate branches (arrows). *Cerebral angiogram.* Prominent right medial lenticulostriate arteries giving a "moyamoya" appearance (**e**, arrow)

In this case, the patient experienced episodes of sudden-onset symptoms with abrupt resolution consistent with TIAs.

In MMD, these neurologic deficits are related to cerebral hypoperfusion [4]. Furthermore, the patient's symptoms were all left-sided and therefore referable to the right cerebral hemisphere. Of note, the patient was left-handed, and accordingly the primary speech centers may have been right hemisphere dominant, with the episodes of expressive dysphasia thereby reflecting pathology affecting the right hemisphere. It is also important to note that the patient's neurological exam was normal with the exception of left lower extremity hyperreflexia, which is seen in MS but can also be attributed to ischemic changes related to long-standing hypoperfusion.

In addition to patient history, imaging studies are important paraclinical tools in evaluating neurological disturbances. While the brain MRI showed white matter changes, these changes lacked morphology and characteristics typical of MS [2]. Interestingly, T2/FLAIR sequences demonstrated watershed lesions, which can be seen in MS but are also common in MMD [8]. Furthermore, gadolinium-enhanced T1 sequences revealed high signal intensity along the leptomeninges of the right cerebral convexity, taking the shape of an "ivy sign" [5]. The "ivy sign" likely reflects slow flow in leptomeningeal collateral vessels and is often seen in MMD [5]—this MRI finding should prompt dedicated vascular imaging. In this case, the brain MRI findings correlated well with the right terminal internal carotid artery narrowing shown on head CTA and corresponding lenticulostriate branches seen on head CTA and cerebral angiogram. The imaging findings in this case align with those reported in other cases of MMD misdiagnosed as MS. In their 2012 case series, Dorfman et al. reported the "ivy sign" seen on gadolinium-enhanced T1 images in four of eight patients with MMD [8]. They also noted watershed white matter lesions seen on T2/FLAIR images in the majority of patients studied [8].

Numerous conditions can mimic MS. One must consider clinical history and paraclinical results when formulating differential diagnoses for MS. Although this patient's age and sex may have supported MS, the clinical features, imaging, and CSF findings were inconsistent with MS. Additionally, while MMD is ten times more common in East Asians than people of Western descent, MMD in the USA demonstrates a predilection for 30–45-year-old Caucasian women [4, 9]. In this case, the incorrect MS diagnosis carried many implications, including delay in appropriate treatment and exposure to potentially harmful disease-modifying therapies. The patient received treatment with interferon beta-1b for 5 years and in addition to the cost of the medication, this placed her at risk for side effects such as lymphopenia and liver function abnormalities [10]. Also, had her primary neurologist decided to escalate treatment to a higher-efficacy MS therapy, the patient could have been at risk for serious complications such as progressive multifocal leukoencephalopathy. In addition to risk related to MS treatment, the patient was also at risk for complications of untreated MMD. Treatment for MMD includes surgical revascularization; however, as in this case, antiplatelet therapy alone may be sufficient in mild MMD [4]. Clinicians should be aware of the clinical and radiological manifestations of vascular syndromes such as MMD, and appropriately consider these in the differential diagnosis of MS.

Funding This case report was supported in part by a grant from the National Multiple Sclerosis Society (RG-1606-08768 to SS).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval For this type of report, formal consent is not required. This article does not contain any studies with animals performed by any of the authors.

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