Neurological Sciences (2019) 40:861–864
https://doi.org/10.1007/s10072-018-3671-0

BRIEF COMMUNICATION

The pathological spectrum behind migraine aura status: a case series

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Received: 17 August 2018 / Accepted: 29 November 2018 / Published online: 6 December 2018

Abstract

Background The recently released International Classification of Headache Disorders—3rd edition (1) includes migraine aura status (MAS) among the complications of migraine (A1.4.5). It is defined as the recurrence of at least three auras over a period of 3 days, in a patient suffering from migraine fulfilling criteria for *1.2 Migraine with aura* (MA) or one of its subtypes.

Case series We describe three cases of MAS secondary to an organic brain lesion: a migrainous infarction, an acute ischemic stroke secondary to a vertebral artery dissection, and an inflammatory demyelinating disease of the central nervous system.

Conclusions In front of a patient with a MAS, an organic lesion of the brain must be suspected, until a complete negative vascular and neuroradiological diagnostic workup has been performed. A spectrum of underlying pathologies (vascular or demyelinating diseases, epileptic or degenerative conditions) may cause a MAS-like clinical onset. The variability of aura symptoms may result in a real diagnostic challenge.

Keywords Migrainous infarction · Ischemic stroke · Inflammatory diseases · Recurrent auras · Spectrum

Abbreviations

MAS	Migraine aura status
MA	Migraine with aura
CT	Computed tomography
MRI	Magnetic resonance imaging
MRA	Magnetic resonance angiography
CTA	Computed tomography angiography

Introduction

Migraine Aura Status (MAS) has been included among the complications of migraine, reported in the Appendix (A1.4.5) of the recently released International Classification of Headache Disorders – 3rd edition (ICHD-III) [1]. This clinical entity, ranging from 1.7 to 4.2% of consecutive patients observed in a tertiary headache outpatient center [2], is now defined as the recurrence of at least three auras over a period of 3 days, in a patient suffering from migraine fulfilling criteria for *1.2 Migraine with aura* (MA) or one of its subtypes. Differently, the previous diagnostic criteria referred to MAS as the recurrence of at least two auras per day for 3 days or more [3]. Here, we report three cases, which are clinically adherent to the new definition of MAS, but concealing completely different etiologies. On their path, we emphasize the need to consider MAS as a potentially threatening clinical condition.

Case reports

Case 1

A 56-year-old woman, with a past medical history of autoimmune hypothyroidism and mood disorders, had suffered from MA during her fertile age. Her attacks were preceded by scintillating scotomas, with a homonymous distribution in her binocular visual field, gradually extending and disappearing along a 30-min duration. Several years before, a brain magnetic resonance imaging resulted unremarkable. Recently, she experienced a 4-year attack-free period. In the last 2 weeks, the patient experienced the return of her well-known MA attacks: her 30-min usual visual auras were followed by a migrainous headache. This time, a few visual symptoms without subsequent head pain were reported. Her auras gradually became more frequent, up to six visual auras a day. She was evaluated at our Headache Centre: the examination revealed

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a right homonymous hemianopia; the computed tomography (CT) brain scan and the brain magnetic resonance imaging (MRI) showed a left occipital ischemic lesion (Fig. 1a–c). Her blood exams were unremarkable, as her cardiological and neurosonological findings were. A diagnosis of migrainous infarction was achieved. The headaches rapidly resolved on treatment with verapamil 120 mg a day in refracted doses, without clinical relapse at a 6-month follow-up examination. Pharmacological prophylaxis is still ongoing. A partial right homonymous hemianopia persisted at the neurological examination.

Case 2

A 32-year-old overweight woman, with a silent past medical history, developed a new headache with migrainous features and a permanent left-sided location, during the last 2 weeks. A cervical contra-lateral pain was present, in absence of recent trauma or cervical manipulations. She had no history of primary headache. She reported visual symptoms described as scintillating scotomas with a right homonymous distribution in her binocular visual field. In the first day, they lasted about 10 min and were followed by a migrainous headache. These auras recurred more than three times a day for the next 3 days, gradually becoming more frequent and finally persistent. An urgent brain MRI revealed a left occipital ischemic stroke (Fig. 1d), while magnetic resonance angiography (MRA) and computed tomography angiography (CTA) showed a full-length dissection of her right vertebral artery (Fig. 1e, f). A diagnosis of acute ischemic stroke caused by spontaneous vertebral artery dissection was achieved.

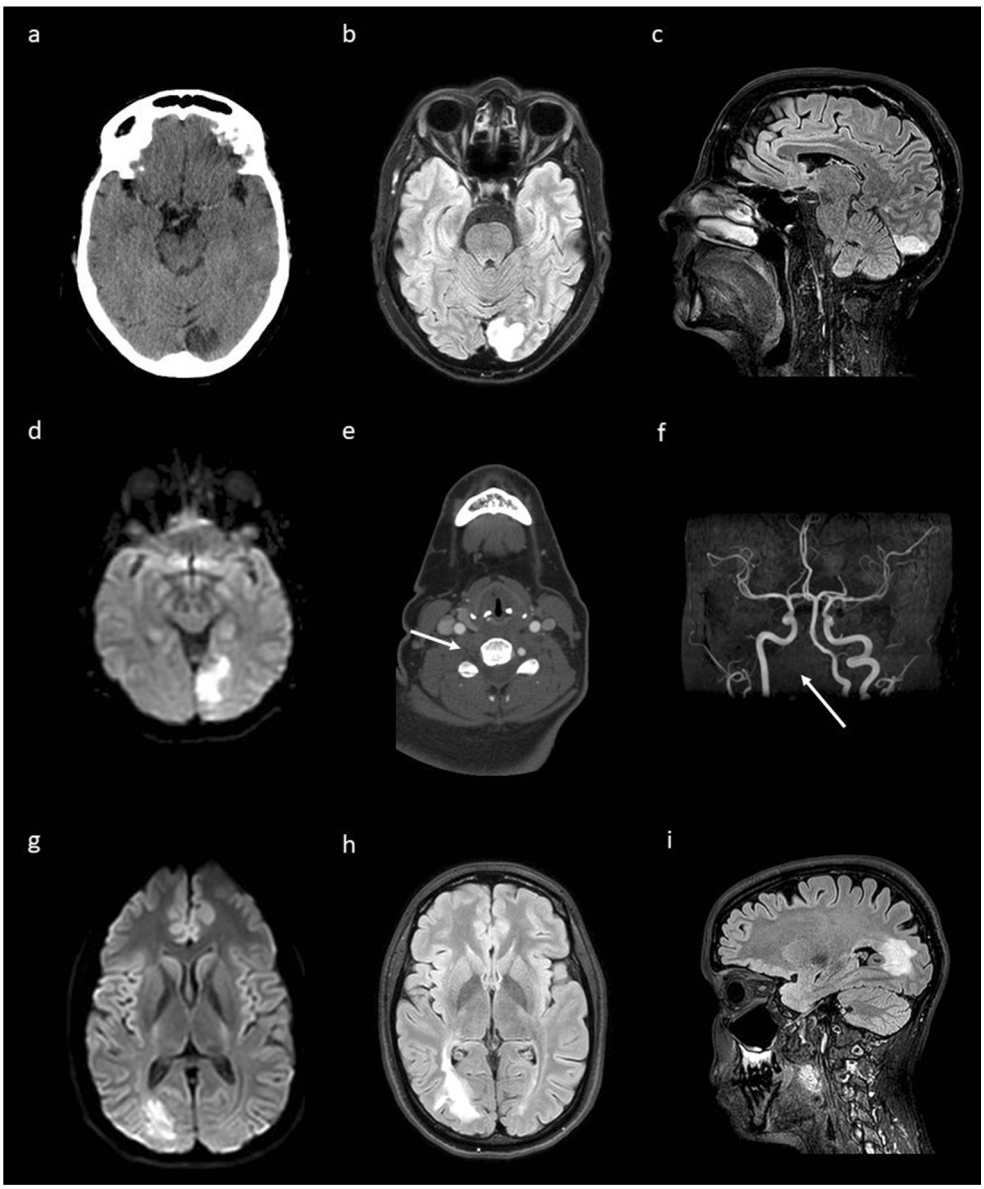

Fig. 1 **a**–**c** Migrainous infarction in a 56-year-old woman: **a** CT brain scan showing left occipital hypodensity; **b** left occipital hyperintensity in axial fluid–attenuated inversion recovery sequence; **c** left occipital hyperintensity in sagittal fluid–attenuated inversion recovery sequence. **d**–**f** Left occipital ischemic stroke due to right vertebral artery dissection in a 32-year-old woman: **d** left occipital hyperintensity in axial diffusion–weighted imaging sequence; **e** CTA showing occlusion of right vertebral artery, not visible (arrow); **f** MRA with no signal from the right vertebral artery (arrow). **g**–**i** Inflammatory disease of the central nervous system with right occipital lesion in a 28-year-old woman: **g** right occipital hyperintensity in diffusion-weighted imaging sequence; **h** right occipital hyperintensity of the white matter in axial fluid–attenuated inversion recovery sequence; **i** right occipital hyperintensity of the white matter in sagittal fluid–attenuated inversion recovery sequence

Case 3

A 28-year-old woman, with a past medical history of post-herpetic trigeminal neuralgia, suffered from MA with occasional attacks heralded by visual symptoms, described as homonymous scintillating scotomas, with reported alternation of the affected side, rapidly evolving towards a parcellar visual field defect. The frequency of her auras was low (about one episode/year); sometimes, their duration was longer than 60 min. A typical migrainous headache followed within 1 h. Six years before, a brain MRI showed only an unspecific little hyperintensity located in the left periventricular parietal region, in fluid-attenuated inversion recovery sequences (FLAIR). She took no continuative oral therapy at home. During the last month, she suffered from recurrent visual symptoms characterized by her well-known scotomas in her binocular visual field: they had a homonymous distribution, but this time, they did not show the usual alternation of side; an inter-critical headache with migrainous pattern was reported. Visual symptoms and headaches became strictly recurrent, without a real symptom-free interval during the last days before admission. A neurological evaluation found a left inferior homonymous defect in her visual field. A new right occipital hypodensity was evident at the urgent brain CT scan. A cerebral MRI revealed multiple areas of alteration of signal involving the periventricular and peri-callosal white matter (Fig. 1g–i). A medullar MRI (normal), the visual evoked potentials (bilaterally slowed down) and a lumbar puncture (lymphocytic pleocytosis, with oligoclonal band), enabled us to achieve the diagnosis of inflammatory demyelinating disease of central nervous system.

Discussion

MAS is a complication of migraine, as reported in the Appendix of the ICHD3 [1]. The frequency of episodes required for its diagnosis has decreased from the ICHD-II [4], through ICHD-III beta [3] to the last revision [1]. The actual temporal criterion refers to at least three auras over a period of 3 days. This modification is probably related to the rare occurrence of previously defined MAS presentation [2]. Our clinical reports aim at underlining what can be hidden behind the new onset of high-frequency aura symptoms (case 2) or behind a brisk increase in their frequency in patients with a previously achieved diagnosis of MA (cases 1 or 3). In both conditions, an organic lesion of the brain must be suspected, especially with abnormalities at the neurological examination, until a complete negative vascular and neuroradiological diagnostic workup has been performed. The brain lesion may be the complication of migraine itself (case 1); in this case, a significant increase in the frequency of auras respect to the baseline of a MA patient is a strong call for a prompt prophylactic therapy, preferably with calcium antagonists [5–7] or lamotrigine [8]. Otherwise, it becomes evident that MAS could be the clinical face of a spectrum of pathological underlying conditions, spreading from ischemic lesions to inflammatory ones. This "secondary" aura status could affect migrainous patients too, more frequently than claimed by some authors [2]. So, achieving a correct diagnosis using only clinical data may be a real challenge: visual aura symptoms last for more than 1 h in 14% of cases (21% and 17% for sensory and dysphasic symptoms respectively) and about a quarter of MA patients experience at least one aura symptom lasting for more than 1 h [9]. The significant variety of visual disturbances and the intra-patient variability of aura phenotype further complicate the diagnostic process [10–13]. From a clinical point of view, in front of a patient with a new onset of MA or with a clear modification of his headache pattern, especially if associated with abnormalities at the neurological examination, a secondary headache must be suspected; if symptoms are suggestive for MAS, we should think about what we may call the migraine aura status spectrum: ischemic lesions, inflammatory diseases, migrainous infarction, epileptic disorders, neoplastic lesions, amyloid angiopathy or subdural hematoma, reversible cerebral vasoconstriction syndrome, and posterior reversible encephalopathy syndrome [1, 2]. All these conditions may provoke a circumscribed and prolonged increase of cortical excitability. A modification in extracellular K^+ signal with a disruption of cell membrane ionic gradients (influx of sodium and calcium), a release of glutamate, an alteration of vasomotor responses with microvascular endothelial dysfunction [14, 15], and a synaptic plasticity alteration (long-term potentiation and decreased inhibitory tone) [16] may explain the early recurrence of aura symptoms [2, 7, 17].

Compliance with ethical standards

Informed consent was obtained from all individual participants included in the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

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