

Migraine-like Visual Aura Rriggered by a Large Aneurysm in the Left Extracranial Internal Carotid Artery with Successful Prevention of Recurrence by the new Anticoagulant Dabigatran: First Case Report

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Abstract-

Purpose: We present a rare case of late-onset migraine-like visual aura triggered by a large aneurysm in the left extracranial internal carotid artery. To the best of our knowledge, this is the first case of migraine-like visual aura triggered by an extracranial internal carotid artery (ICA) aneurysm. This is also the first case of migraine-like visual aura with probable thromboembolic trigger being successfully treated with a new anticoagulant, dabigatran.

Case Report: A 61-year-old woman complained about stereotypical episodes of a short-lasting flickering light in the right visual field for about half a year. Magnetic resonance imaging (MRI) of the head revealed a large aneurysm arising from the mid-cervical portion of the left internal carotid artery (ICA). After anticoagulant therapy with 110 mg of dabigatran twice a day, she became free from the visual symptom.

Conclusion: Late-onset migraine with aura, especially typical aura without headache should be diagnosed carefully since it can be a challenge to distinguish it from signaling something serious. Micro-thromboembolism, commonly cardiogenic, but rarely arising from a carotid aneurysm, can trigger cerebral ischemic injury, causing transient neuronal hyperexcitability and cortical spreading depression (CSD)-like “spontaneous” waves propagating through the penumbra of the injured region into normally perfused tissue. The resultant symptoms may semiologically mimic visual aura. Migraine-like visual aura in this patient was successfully treated with dabigatran. It may not only imply that the patient’s migraine-like visual aura was a thromboembolic event, but may also suggest the potential efficacy of the new anticoagulant, dabigatran, as the optimal alternative of warfarin in treating a thromboembolic event arising from a carotid aneurysm.

Key Words: Carotid aneurysm, migraine with aura, cortical spreading depression, transient ischemic attack, dabigatran

Acta Neurol Taiwan 2015;24:19-24

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Received April 25, 2014. Revised June 11, 2014.

Accepted Ougust 21, 2014.

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INTRODUCTION

Migraine with aura is defined by the third edition (beta version) of The International Classification of Headache Disorders (ICHD-3 beta)⁽¹⁾ as follows. Migraine with aura, in which the aura consists of visual and/or sensory and/or speech/language symptoms, but not motor weaknesses, and characterized by gradual development, a duration of each symptom no longer than an hour, a mix of positive and negative features, and complete reversibility (Table 1). About 20 to 25 percent of people with migraine experience aura, more than 90 percent of which are visual⁽²⁾. There are numerous reports about secondary causes provoking headache or aura that are clinically indistinguishable from primary headache syndromes. Migraine-like visual aura has been associated with various cardiac and cerebral structural abnormalities⁽³⁾. Never has migraine-like visual aura been reported as resulting from an internal carotid artery (ICA) aneurysm. In this paper, we present a 61-year-old woman experiencing late-onset episodic migraine-like visual aura triggered by a large aneurysm in the left

extracranial ICA. Besides, to the best of our knowledge, this is also the first case report about a successful treatment of migraine-like visual aura of potential thromboembolic cause with a new anticoagulant, dabigatran.

CASE HISTORY

A 61-year-old Chinese Malaysian woman had a history of frequent episodic migraine without aura since her age of 20s. She described her headaches as throbbing headaches of moderate to severe intensity in the bilateral temporo-occipital region and that the headaches were aggravated by physical effort. Her headaches were often accompanied by nausea and occasional vomiting. There was phonophobia without photophobia during the headache period. The headaches usually lasted all day and would not subside until analgesics were used. She had to tolerate at least 4 to 6 days of headache attacks per month during her early years as a laborer in Malaysia. A marked decrease in frequency of headaches has been observed since her stay in Taiwan with her daughter 2 years ago.

Table 1. The International Classification of Headache Disorders, the third edition (beat version) (ICHD-3 betaa)

1.2	Migraine with aura
	A. At least two attacks fulfilling criteria B and C
	B. One or more of the following fully reversible aura symptoms:
	1. visual
	2. sensory
	3. speech and/or language
	4. motor
	5. branstem
	6. retinal
	C. At least two of the following four characteristics:
	1. at least one aura symptom spreads gradually over > 5 minutes, and/or two or more symptoms occur in succession
	2. each individual aura symptom lasts 5-60 minutes *
	3. at least one aura symptom is unilateral §
	4. the aura is accompanied, or followed with in 60 minutes, by headache
	D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.
1.2.1.2	Typical aura without headache
	A. Fulfils criteria for 1.2.1 Migraine with typical aura
	B. No headache accompanies or follows the aura within 60 minutes.

*: When, for example, three symptoms occur during an aura, the acceptable maximal duration is 3x60 minutes. Motor symptoms may last up to 72 hours.
§: Aphasia is always regarded as a unilateral symptom; dysarthria may or may not be.

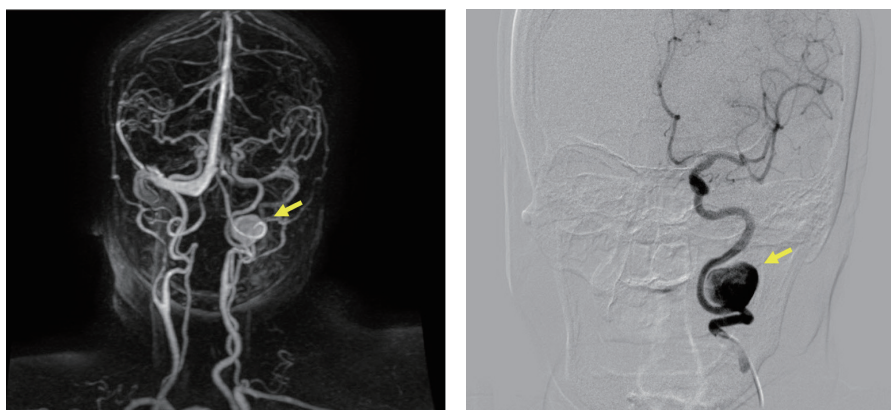


Figure 1. (A) The magnetic resonance angiography (MRA) revealed a large aneurysm from the mid-cervical portion of the left ICA. (B) The cerebral DSA confirmed a 23x21mm big aneurysm (neck about 5-6mm) in the left mid-cervical ICA with a downward opening and an upward-facing dome.

She started to experience episodic flickering lights in the right visual field of both eyes about half a year before her presentation at the outpatient clinic of Chung Shan Medical University Hospital. Happening nearly every day, each attack of visual symptom was stereotypical, with an abrupt onset within 1 to 2 seconds and lasting about 10 to 15 minutes followed by a spontaneous remission without any headache occurring within 60 minutes. Between episodes, she was free of symptoms. The ophthalmic checkup confirmed normal results before this neurological interview. At the first visit her blood pressure was 113/67 mmHg, heart rate was regular at 72 beats per minute, and general physical and neurological examinations were normal.

Her symptoms can not fulfill the ICHD-3 beta criteria for migraine with aura and its subtype, typical aura without headache, unless transient ischemic attack and other better accounts in ICHD-3 diagnosis can be excluded. Our recommendation was to rule out other causes because red-flag symptoms existed – a very short onset of visual symptoms, a stereotypical pattern, and an onset of symptoms over the age of 40.

We therefore arranged magnetic resonance imaging (MRI) of the head. It surprisingly revealed a large aneurysm, about 22 mm in diameter, arising from the mid-cervical portion of the left ICA. There were nothing more than a few small gliosis lesions in the subcortical region of bilateral frontal lobes. The patient confirmed her

experience of a major head trauma in her 30s that might have contributed to this big carotid aneurysm. Further investigation with cerebral digital subtraction angiography (DSA) confirmed a 23x21mm big aneurysm (neck about 5-6mm) with a downward opening and an upward-facing dome at the left mid-cervical ICA.

As a Malaysian without health insurance in Taiwan, she was not able to afford surgical or endovascular interventions. Medical treatment with anticoagulant was strongly recommended to prevent potential thromboembolism resulting from the aneurysm. Worried about bleeding and other adverse effects of warfarin, the patient chose to use a new oral anticoagulant, dabigatran, and took 110 mg twice a day. We had followed the patient for 5 months until she received endovascular intervention with flow-diverting stent. She reported that she had never experienced any visual symptom since the day she started anticoagulant therapy.

DISCUSSION

This 61-year-old woman was experiencing a new onset of episodic migraine-like visual aura for about half a year. Her visual symptoms semiologically met the ICHD-3 beta criteria for migraine with aura and its subtype, typical aura without headache, only if transient ischemic attack and other accounts in ICHD-3 diagnosis can be excluded. According to the comments from ICHD-3 beta

in Section 1.2.1.2, typical aura without headache, as to the absence of headaches, it is difficult to make a precise diagnosis of the aura and to distinguish it from mimics that may signal serious disease (e.g., transient ischemic attack); further investigation is often required. When the aura occurred for the first time after age 40, when symptoms were exclusively negative (e.g., hemianopia), or when the aura was prolonged or very short, other causes, particularly transient ischemic attacks, should be ruled out. According to a literature review on migraine-like visual aura due to focal cerebral lesions,⁴ the red-flag warning features of the visual aura are stereotypical visual aura, increasing frequency of visual aura, change in the pattern or characteristics of chronic visual aura, any unexplained visual field defects, and negative visual phenomena or subjective persistence of a scotoma following a typical visual aura.

In this patient, the reasons for neuroimaging to exclude secondary causes of migraine-like visual aura include:

1. The age of onset after 40.
2. Very short onset of the visual symptom.
3. Stereotypical visual symptoms locked on the right visual field.

Never has migraine-like visual aura been reported in association with an extracranial ICA aneurysm. There are many case series and case reports about secondary causes of migraine with aura. Among them, cardiac abnormalities are the most common cause, including patent foramen ovale (PFO), atrial septal defect (ASD), atrial septal aneurysm, mitral valve prolapse, congenital heart disease, pulmonary shunt, and cardiac myxoma⁽³⁾. Other non-cardiac causes that have been reported are transient ischemic attack⁽⁵⁾, intraventricular tumour,⁶ arteriovenous malformation⁽⁷⁻¹¹⁾, midbrain cavernous malformation⁽¹²⁾, brain abscess⁽¹³⁾, cerebral venous thrombosis,¹⁴ vertebral artery dissection⁽¹⁵⁾, cerebral primary tumor or brain metastasis⁽¹⁶⁻¹⁸⁾, and rupture of middle fossa arachnoid cyst⁽¹⁹⁾.

Calcium dysregulation, abnormal concentrations of GABA, glutamate, magnesium, nitric oxide, potassium and abnormalities in arachidonic acid, prostaglandin, and mitochondrial oxidative phosphorylation have all been postulated in the pathogenesis of migraine and aura⁽⁴⁾. Cortical spreading depression (CSD) can also be induced

by elevated extracellular potassium, glutamate, and inhibition of Na⁺/K⁺ adenosine triphosphatase⁽²⁰⁾. There is also evidence suggesting that ischemic injury to the human brain can generate “spontaneous” waves propagating through the penumbra of cortical infarcts into normal tissue resembling the characteristics of CSD⁽²¹⁾.

The mechanism to trigger migraine-like visual aura in our patient is assumed to be microemboli arising from the left extracranial ICA aneurysm, spreading to the left cerebral cortex, resulting in transient cerebral ischemia and hyperexcitability of the cortical neurons, generating CSD-like waves, and finally giving rise to migraine-like visual aura stereotypically “locked” in the right visual field.

Extracranial ICA aneurysm is an uncommon and serious condition. The reported incidence is 0.09 ~ 2.0% in all carotid surgical procedures⁽²²⁾. Most extracranial ICA aneurysms are asymptomatic and detected coincidentally. Asymptomatic patient are believed to remain asymptomatic and may be followed periodically without invasive treatment⁽²³⁾. An extracranial ICA aneurysm may present most commonly with central neurologic symptoms due to cerebral embolism but might also present with local compression causing cranial nerve function loss or dysphagia⁽²²⁾. Symptomatic patients with extracranial ICA aneurysms usually receive invasive treatment because of the assumed high morbidity and mortality rate if left untreated⁽²⁴⁾. There are several surgical approaches according to the anatomy and accessibility of the extracranial ICA aneurysms and a newly-developed flow-diverting stenting procedure. Since there are no evidence-based guidelines, practitioners have to depend on gained experience and indication based on the location and etiology described in the available literatures.

In the view of a potential thromboembolic cause of migraine-like visual aura in this patient, we suggested the use of anticoagulant therapy for the patient. Worried about the bleeding risk of warfarin and the difficulty in keeping medical follow-up appointments because of her lack of health insurance in Taiwan, she decided to try a new anticoagulant, dabigatran. Acting as a direct thrombin inhibitor, dabigatran is approved by the Food and Drug Administration, Ministry of Health and Welfare of Taiwan, and Drug and Food Administration (FDA) of the United States to treat patient with non-valvular atrial fibrillation in prevention of stroke and systemic

embolism. It is also approved by the FDA of Canada for postoperative thromboprophylaxis after surgical knee and hip replacement. Despite the lack of evidence of the efficacy in preventing thromboembolic events caused by an aneurysm of internal carotid artery, there are some case reports about dabigatran successfully treating non-atrial fibrillation cardiac or non-cardiac thromboembolic events⁽²⁵⁾. The patient saw dramatic benefit from the medical treatment. Furthermore, the effectiveness of the anticoagulant also indirectly confirmed the hypothesis of micro-thromboembolism causing migraine-like visual aura in this patient.

CONCLUSION

We demonstrate a rare case of migraine-like visual aura triggered by probable micro-thromboembolism arising from a big left extracranial ICA aneurysm. "Red-flag" symptoms of a patient with visual aura should always warrant a detailed investigation to look for unusual secondary causes. Many cerebral and cardiovascular structural diseases have been reported in association to migraine with aura. Most of the causes can be attributed to micro-thromboembolism and the resultant cerebral hyperexcitability. Despite lacking evidence of dabigatran preventing thromboembolism in ICA aneurysm, we successfully halted the attacks of migraine-like visual aura with such a novel anticoagulant. Further studies may be needed to confirm whether dabigatran can be an optimal alternative of warfarin in treating thromboembolism arising from an extracranial internal carotid aneurysm.

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