Atypical Symptoms in Migraine-Related Alice in Wonderland Syndrome: Expansion of the Phenotype and Reflection on the Pathomechanism

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ABSTRACT

We report an 8-year-old girl who experienced daily episodes of visual and somesthetic distortion and was diagnosed with Alice in wonderland syndrome (AIWS). Ophthalmologic assessment revealed best-corrected visual acuity of 0.2 in both eyes, and bilateral constricted tubular or spiral visual fields. Augmented amplitude of visually evoked potentials was revealed, and treatment with lomerizine and valproate showed favorable effect on the visual/somesthetic distortion as well as the visual field and acuity. Psychogenic visual problems can co-exist with the typical sensory distortion in AIWS, similarly to the case of psychogenic pseudo-seizures in subjects with epilepsy. Otherwise, an ambiguous borderline between psychological and physical pathomechanisms in migraine may also be characteristic of the migraine-related AIWS.

Key words Alice in Wonderland syndrome; dissociation; migraine; psychogenic visual disturbance

Alice in wonderland syndrome (AIWS) is characterized by the constellation of visual and somesthetic distortions. These could be often misdiagnosed as psychogenic visual disturbance in general physicians. In addition, we recently experienced a case with AIWS, where co-existence of "psychogenic" visual disturbances and AIWS symptoms made the diagnosis confusing. This aspect may be misdiagnosed even by experienced child neurologists and ophthalmologists. Herein we delineate the clinical features of this case for acknowledgements to the readers.

PATIENT REPORT

An 8-year-old girl suffered from pressure-type daily headaches in her vertex, lasting for 1 h. During this period, she developed the following episodic symptoms lasting for up to 5 min: (i) seeing objects larger (macropsia) or smaller (micropsia) than they were originally, (ii) difficulty in walking because of seeing legs of others to be closer in her path (proxiopia), (iii) seeing her mother's face in four copies (polyopia), (iv) differently seeing colors of objects, such as crayons and traffic signals (dyschromatopsia), (v) blistering objects in her eye field, (vi) seeing or somesthetically feeling her own body below the neck as transparent or absent, (vii) feeling hot foods in her mouth as colder, and (viii) altered experience of phychological time (time distortion). Besides, she had transient abdominal pain. Although dyschromatopsia appeared daily, other symptoms emerged a couple of times per week. Her headaches did not demonstrate temporal correlation with these episodic symptoms.

The girl presented with a friendly, talkative, and expressive character at medical referral from a local ophthalmologic clinic with a suspicion of psychogenic visual disturbance. Upon examination at 9 years, the position sense in her short toes and the vibration sense in her arms and feet had declined. Her best-corrected visual acuity (BCVA) was 0.2 in both eyes. The bilateral constricted tubular visual fields within 10° or spiral visual fields and color vision deficiency were revealed on repeated examinations; however, no organic diseases were diagnosed through a general ophthalmic investigation. Both magnetic resonance imaging and electroencephalography displayed unremarkable results. The serological examination demonstrated negative results for Epstein–Barr virus (EBV) infection. Pattern-reversal visually evoked potentials (VEPs) were augmented in amplitude, and somatosensory evoked potentials from the median, ulnar, and sural nerves were normal (Figs. 1A and C). The girl was diagnosed with AIWS based on the symptoms of visual and somesthetic distortions, despite the presence of atypical findings of spiral/tubular vision and impaired deep sensation. Thus, lomerizine at 10 mg/day was initiated at the request of the girl and her mother, resulting in the immediate disappearance of episodic symptoms other than dyschromatopsia. However,

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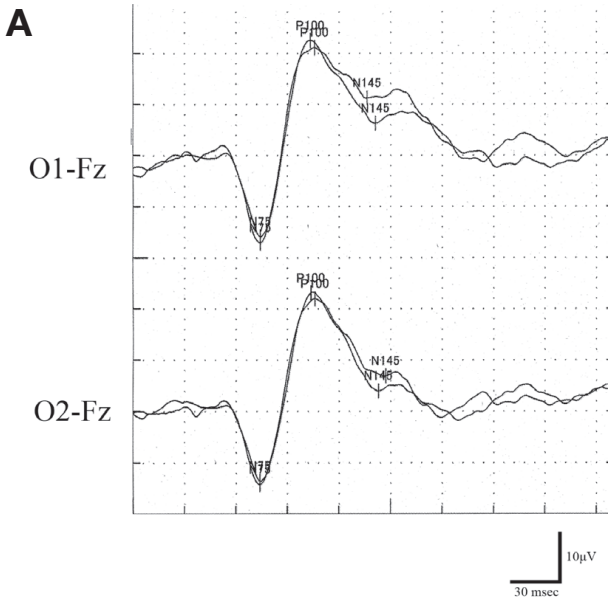
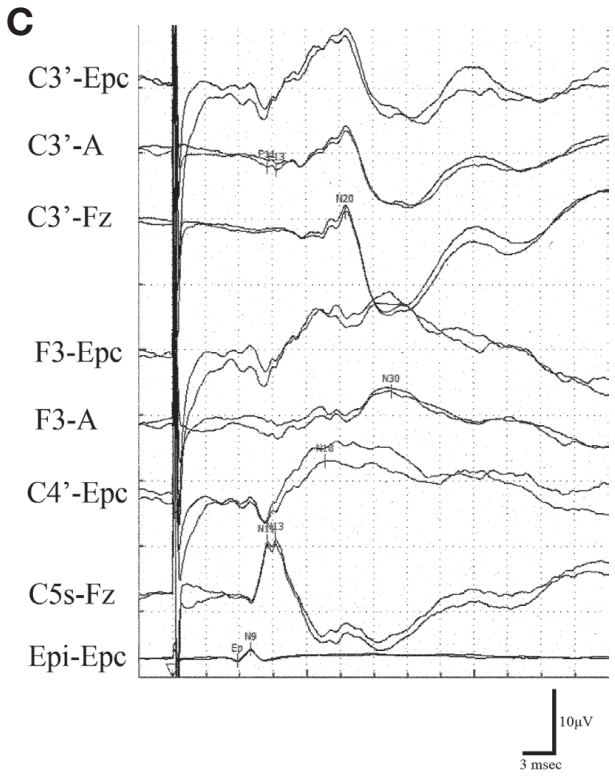
Received 2018 December 10
Accepted 2019 February 18
Abbreviations: AIWS, Alice in wonderland syndrome; BCVA, best-corrected visual acuity; EBV, Epstein–Barr virus; VEP, visually evoked potential





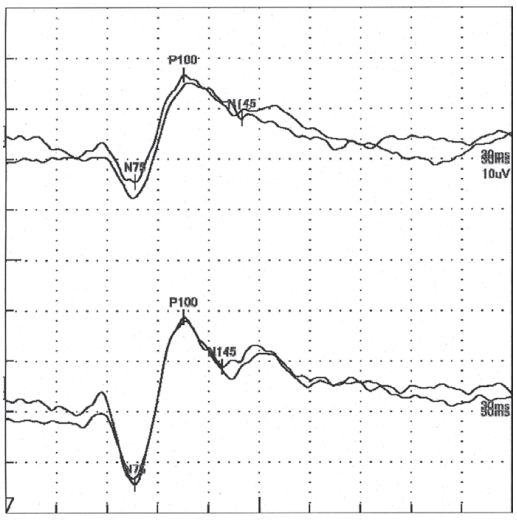


Fig. 1. Visual (**A** and **B**) and somatosensory (**C**) evoked potentials of the patient at the age of 9 years and 5 months (**A** and **C**) and 2 months later under medication with lomerizine and valproate sodium (**B**). The right median nerve was stimulated for somatosensory evoked potentials. A: potential of electrically linked both ears; C3', C4': location 2 cm posterior to C3 and C4, respectively. Epc, Erb's point contralateral to the stimulation; Epi, Erb's point ipsilateral to the stimulation; Fz, midline frontal.

the addition of valproate sodium (VPA) at 400 mg/day for 3 weeks did not further resolve the symptom. After 1 month, the amplitude of VEP was reduced (Fig. 1B).

Although micropsia once per month and occasional dyschromatopsia persisted, they were completely resolved within 5 months of medication, accompanied by the recovery of BCVA to 1.2 in both eyes. In addition, visual field and color tests revealed normal results. Vibration sense was normal in follow-up examinations.

Two months after the initiation of VPA, the girl experienced daily pulsatile headaches lasting for up to several hours, with unilateral distribution, nausea, photophobia, and avoidance of routine physical activity, which fulfilled the diagnosis of a migraine without aura.[1] The father of the patient had a history of migraine. Treatment with amitriptyline and propranolol, along with the termination of lomerizine and VPA after the resolution of visual/somesthetic symptoms, yielded a stable state with rare, yearly headaches. Distorted vision of written letters transiently reappeared at the age of 11 years. The intelligence quotient of the girl was assessed as 102 using the Wechsler Intelligence Scale for Children-IV at the age of 10 years.

DISCUSSION

Etiologies responsible for the symptoms of AIWS in childhood are diverse, but are mostly attributed to epilepsy, migraine and EBV infection.[2] For the present patient, the episodes of visual and somesthetic distortion and the development of migraine without aura later in the clinical course, support the diagnosis of migraine-associated AIWS.[3] In addition, augmented amplitude of VEP and its amelioration after the resolution of symptoms of AIWS have also been reported in AIWS,[4] which has not been consistently proven in migraine. AIWS patients have shown regional cortical dysfunction in either occipital-parietal, occipital-temporal or frontal-parietal areas on functional neuroimaging.[5–9] Interestingly,

abnormal perfusion or metabolism were identified in the parietal lobes of patients with visual distortion of size or shape of objects, and in the temporal lobe of a patient with color misrecognition.[9] The abnormal parietal and temporal association cortex corresponded to the dorsal and ventral stream of high-level visual processing, respectively. The effect of calcium blockers on AIWS symptoms is assumed to result from mitigation of hyperactivation in these streams, and the predominance and persistence of dyschromatopsia in the present patient may represent a differential severity of dysfunction between the dorsal and ventral streams. In terms of the augmented VEP amplitude, early components of N75 and P100 represent the activity provoked in the primary (or secondary) visual area,[10, 11] and do not directly correspond to the dysregulation of the higher association areas. These early potentials are rather indicators of excitation in surrounding visual association areas. In contrast, blistering objects in the eye field and thermal distortion in the mouth are unusual symptoms in AIWS, and the effect of calcium blockers on these symptoms needs further confirmation. However, these may be characteristic in certain migraine-related AIWS and are worth recognition.

Conversely, concentric or spiral visual fields, poor visual acuity without causative lesions suggest that some of the complaints by the present patient may have represented psychogenic factors in her symptoms. AIWS symptoms can accompany background psychological conditions of depression, dissociation, and schizophrenia.[2] In turn, subjects with AIWS may be susceptible to other visual/somesthetic aspects of dissociative or conversion disorders, e.g., concentric or spiral visual fields and impaired vibration/position sense experienced in the present patient. This issue may be linked to the question why certain children with migraine suffer from AIWS. Although not apparent and not scrutinized in the present patient, certain background traits may play a role in the development of migraine-related AIWS, e.g., autism spectrum disorders or borderline personality disorder, both of which are often accompanied by conversion symptoms.

On the other hand, visual symptoms of AIWS are known to arise several seconds after visual fixation.[4] This may represent an attention-induced augmented activity in the visual association area and other extrastriate cortex, which can be identified in the augmented amplitude of visual event-related potentials in their components later than 100 ms.[10, 12] Such a mechanism may be reflected in the situation-sensitive emergence of symptoms of AIWS on medical examination. At least, poor visual acuity might be explained by the provocation of optic allesthesia (inverted vision) in the strained settings of an ophthalmologic clinic. Notably, physical and mental stress influences the emergence and aggravation of migraine headaches, which underscores an ambiguous borderline between psychological and physical pathomechanisms in migraine and its equivalents. This may also be applicable to AIWS.

Thus, unusual symptoms initially interpreted as psychogenic might be experienced or explained in the context of AIWS. It is warranted that children with AIWS should be assessed and followed up carefully under the collaboration of ophthalmologists, child neurologists, and pediatric psychiatrists.

The authors declare no conflicts of interest.

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