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Original Article

"Alice in Wonderland" Syndrome: Presenting and Follow-Up Characteristics

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ABSTRACT

BACKGROUND: We investigated the distribution of symptoms and etiologies of patients with "Alice in Wonderland" syndrome (visual perception of change in one's body size) and "Alice in Wonderland"–like syndrome (extrapersonal illusions) at presentation and to determine their prognosis. **DESIGN:** Retrospective chart review and telephone interview. **METHODS:** Charts of children diagnosed with "Alice in Wonderland" syndrome by a pediatric neuro-ophthalmologist between July 1993 and July 2013 were reviewed. Patients seen before 2012, or their parents, were contacted for follow-up information. **RESULTS:** A total of 48 patients (average age 8.1 years) diagnosed with "Alice in Wonderland" syndrome or "Alice in Wonderland"–like syndrome were identified. Common visual symptoms were micropsia (69%), teleopsia (50%), macropsia (25%), metamorphopsia (15%), and pelopsia (10%). Magnetic resonance imaging and electroencephalography were unrevealing in 21 of 21 and 23 of 23 cases, respectively. The etiology was infection in 33% of patients and migraine and head trauma in 6% each. No associated conditions were found in 52%. Of the 15 patients with follow-up, 20% had a few more events of "Alice in Wonderland" syndrome or "Alice in Wonderland"–like syndrome, which eventually stopped after the initial diagnosis; 40% had no more events, and 40% were still having "Alice in Wonderland" syndrome or "Alice in Wonderland"–like syndrome symptoms at the time of the interview, while four patients (27%) developed migraines and one patient (7%) seizures since the diagnosis. **CONCLUSION:** "Alice in Wonderland" syndrome and "Alice in Wonderland"–like syndrome typically affect young children, and the most common visual complaints are micropsia and teleopsia. The most common associated condition is infection, but half of these individuals have no obvious trigger. Magnetic resonance imaging and electroencephalography are not helpful. The symptoms of "Alice in Wonderland" syndrome and "Alice in Wonderland"–like syndrome usually resolve, but in more than one third of the cases, they continue. One quarter of patients without a history of migraine may subsequently develop migraine.

Keywords: Alice in Wonderland syndrome, teleopsia, pelopsia, migraine

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Introduction

Patients with the "Alice in Wonderland" syndrome (AWS) experience hallucinations or illusions of expansion, reduction, or distortion of body image.[1] The name comes from the classic story of *Alice's Adventures in Wonderland*, written by Lewis Carroll (Charles Lutwidge Dodgson) in 1865.[2] Lippman[3] first described AWS, and subsequently Todd[4] gave the condition its name.

Individuals with true AWS perceive their own body parts changing size. Lanska et al.[5] referred to this as "type A" AWS. Micropsia (objects appear too small), macropsia (objects appear too large), metamorphopsia (objects appear too fat, thin, short, tall, and so on), teleopsia (objects appear further away than they are), and pelopsia (objects appear closer than

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they are)[1] are extrapersonal visual complaints similar to AWS. Lanska et al.[5] referred to them as "type B." Lanska et al.[5] categorized "type C" complaints as altered perception of one's body image and externally other people or objects as well. To distinguish self versus extrapersonal illusions, for the purposes of this study we will term types B and C as "Alice in Wonderland"–like syndromes (AWLS). Other authors[6] have also advocated this distinction.

The cause of AWS and AWLS is not known. Various authors however have attributed the condition to migraine, epilepsy, and infection. Lippman's[3] seven patients experienced migraine headaches with altered perception of body image. The migraines occurred before, during, or after the AWS symptoms.[3] Three of Todd's[4] six patients had a family history of migraine and/or epilepsy. Golden's two patients with AWS had repeated headaches and a strong family history of migraines.[7] In addition, Copperman[8] presented three cases with AWS as a presenting symptom of infectious mononucleosis.

The purpose of this report is to investigate the distribution of symptoms and associated factors of AWS and AWLS at presentation. Aside from one large meta-analysis,[5] this information is not available for a large series, particularly a pediatric one. The secondary aim was to determine the prognosis of these patients, because most studies focused only on the presenting AWS and AWLS symptoms and neither monitored these patients after the initial onset nor ascertained whether other neurological diseases developed.

Methods

Eligible study participants included children between 1 and 18 years of age seen in a pediatric neuro-ophthalmology practice at the Children's Hospital of Philadelphia from July 1993 to July 2013 who were diagnosed with AWS. These children were identified by searching a master list of pediatric patients seen by a single physician (G.T.L.).

For the prospective portion of the study, to insure an adequate time for follow-up, only those patients seen before 2012 from the eligible list of patients mentioned previously were considered. Telephone contact information for the patients, patients' parent(s) and/or guardian(s) was obtained from the medical record and used to contact the patient (if aged >18 years), parent(s), and/or guardian(s). Informed consent for enrollment in the study was obtained from patients and their parents and/or guardians via telephone. Enrolled participants then answered a brief predrafted telephone questionnaire. The patients (or parents of the patients) were asked if the AWS or AWLS symptoms persisted after the initial diagnosis, if there were new visual symptoms, if the patient was subsequently diagnosed with migraines and/or seizures, if there were any new major medical and/or neurological problems that developed, and if there had been additional testing after the initial diagnosis.

For the retrospective portion of the study, charts from the following groups of patients were reviewed: (1) those who participated in the prospective portion of the study; (2) eligible study candidates who could not be reached by telephone after three consecutive attempts or because their contact information was no longer valid—a waiver of consent was obtained from the Children's Hospital Institutional Review Board for their participation; and (3) patients seen in 2012 and 2013.

Charts for the retrospective portion of the study were reviewed for the following information: date of birth; date of initial visit; sex; relevant medical conditions; whether they experienced teleopsia, pelopsia, micropsia, macropsia, metamorphopsia, other illusions, or true AWS; history of migraines; family history of migraines; history of seizures; neuro-ophthalmic examination findings including refraction and dilated fundus examination; results of brain magnetic resonance imaging (MRI), brain computed tomography, or electroencephalography (EEG); and etiology of AWS or AWLS (migraine, seizure, infection, or other cause). Migraine was defined as headache with any of the following: classic visual aura, photophobia, phonophobia, nausea, vomiting, or abdominal migraine. A family history for migraine was considered positive if a first-degree relative had migraine. Infections included streptococcus, flu-like illnesses (fever, malaise), gastrointestinal illnesses (nausea, vomiting), and upper respiratory illnesses.

The MRI or computed tomography result was considered unremarkable if normal or if only incidental abnormalities (cysts; small, nonenhancing, nonperiventricular, white matter lesions; or venous anomalies, for instance) were found and no mass lesions, infarcts, or hemorrhages were found that may have caused a seizure or visual complaint. The neuro-ophthalmic examination was considered unremarkable if causes of visual distortion were excluded by documentation of a normal anterior segment and fundus examination and no or minimal astigmatism was evident on cycloplegic refraction performed at the time of the examination or by a referring pediatric ophthalmologist. In particular the maculae were examined carefully to exclude a retinal cause of metamorphopsia.

The cause of AWS and AWLS was determined to be migraine when the individual's visual complaints occurred in association with a headache, seizure if the visual complaints had an EEG correlate on random or ambulatory monitoring, or infection if the visual complaint occurred within days of the illness.

This study was conducted in full accordance with all applicable Children's Hospital of Philadelphia research policies and procedures and all applicable federal and state laws and regulations including 45 code of federal regulations (CFR) 46.

Results

Forty-eight patients between 1 and 18 years of age were diagnosed with AWS between July 1993 and July 2013. Records were available for all 48 patients for the retrospective portion of the review. All patients had a normal neuro-ophthalmic examination without significant astigmatism or macular disease. Table 1 summarizes the patient demographics, visual and other symptoms, relevant medical and family histories, test results, and etiologies for these 48 patients.

Twenty-eight patients were seen before 2012 and were therefore eligible for the prospective portion of the study. Fifteen of the 28 patients (54%) and/or parents completed the telephone interview. Four individuals were who did not choose to complete the phone interview did not decline to participate in the retrospective portion of the study. Nine patients could not be reached—three because the contact information was no longer valid and six because contact could not be made in spite of three attempts.

Of the 15 people who were interviewed, the interval between initial diagnosis and telephone contact was 2.1-13.5 years, with an average of 6.5 years (Table 2). Three patients (20%) had a few more events of AWS or AWLS after initial diagnosis, but these eventually stopped. Six patients (40%) had no more events. Six patients (40%) were still having AWS or AWLS symptoms at the time of the interview. Two of these six patients developed new visual symptoms: one patient mixed up numbers and saw figures and shapes that were not there; another patient viewed things as moving in a wave-like sort of motion and had a feeling of things moving. Four patients (27%) who did not have migraines at the initial diagnosis developed migraines later. One patient (7%) had a seizure after the diagnosis. One patient (7%) was subsequently diagnosed with attention-deficit disorder. Five parents (33%) of affected patients stated that they had experienced AWS or AWLS symptoms.

TABLE 1.
Patient Characteristics of Retrospective Study (n = 48)

Features	Numbers	Comments/Examples
Demographics		
Average age at presentation	8.1 yr	Range: 5-14 yr
Number of male patients, n (%)	35 (73%)	
Number of female patients, n (%)	13 (27%)	
Visual symptoms, n (%)		Some patients had multiple symptoms
Teleopsia	24 (50%)	
Pelopsia	5 (10%)	
Micropsia	33 (69%)	
Macropsia	12 (25%)	
Metamorphopsia	7 (15%)	
Movement/shaking	3 (6%)	
Objects in three dimensions	1 (2%)	
Change in one's body image	3 (6%)	
Other related symptoms	1 (2%)	Sounds much louder than normal
History, n (%)		
Migraine	7 (15%)	2 had abdominal migraine only
Migraine in family	22 (46%)	
Seizures	1 (2%)	
AIWS in family	1 (2%)	
Other	4 (8%)	Asperger syndrome, ADHD, Tourette syndrome, prematurity
Tests, n/total n		
Normal MRI	20/21	
Abnormal MRI	1/21	Consistent with preterm birth
Normal EEG	22/23	
Abnormal EEG	1/23	Absence seizures (unrelated)
Other conditions with AWS/AWLS, n (%)		(Some patients had multiple)
Migraine	3 (6%)	
Seizure	0 (0%)	
Infection	16 (33%)	Viral illness, streptococcal sore throat
Head trauma	3 (6%)	
Lack of sleep	1 (2%)	
Lights	2 (4%)	Fluorescent, strobe
Foods	1 (2%)	
None	25 (52%)	

Abbreviations:
ADHD = Attention-deficit/hyperactivity disorder
AIWS = "Alice in Wonderland" Syndrome
AWLS = "Alice in Wonderland"–like syndrome
AWS = "Alice in Wonderland" syndrome
EEG = Electroencephalography
MRI = Magnetic resonance imaging

TABLE 2.
Patient Characteristics of Prospective Study (n = 15)

Interval between initial diagnosis and telephone contact	
Range	2.1-13.53 yr
Average	6.5 yr
AWS/AWLS symptoms	
More events after diagnosis but eventually stopped	3 (20%)
No more events	6 (40%)
Still having events at time of interview	6 (40%)
Medical conditions that developed after initial diagnosis of AWS/AWLS	
Migraines	4 (27%)
Seizures	1 (7%)
ADD	1 (7%)
Parents with AWS/AWLS symptoms	5 (33%)

Abbreviations:
ADD = Attention-deficit disorder
AWLS = "Alice in Wonderland"–like syndrome
AWS = "Alice in Wonderland" syndrome

Four of these parents indicated that they had had these symptoms since childhood. These four parents did not realize until after their child's initial visit and diagnosis of AWS or AWLS that they also had a similar condition.

Discussion

The prospective portion of our study revealed the following: the prognosis for further AWS or AWLS episodes varies from individual to individual. For some patients there were no additional episodes after the initial diagnosis, while others had a few more episodes which eventually resolved. Several patients' symptoms, however, persisted, sometimes in varied forms. After the initial diagnosis, the development of seizures was rare, but development of migraine was common. No other major medical, neurological, or psychiatric problems subsequently developed (only one person had attention-deficit disorder). There was a family history of AWS or AWLS in a portion of the patients, and these individuals may have had a genetic component.

The important findings from the retrospective part of the study are as follows. Most patients had teleopsia and micropsia. Very few had the true AWS. Most patients were male. Almost half had a family history of migraine. Among patients tested, almost all had a normal MRI or EEG result. The most commonly identified associated condition was infection, but more than half the patients had no obvious cause.

Most of our results corroborate the findings of the meta-analysis of Lanska et al.[5] and the smaller series of Weidenfeld et al.[9] The average age of our patients is 8.1 years, and median is 7.9 years, which is very similar to the median age of type B patients reported by Lanska et al.[5] (7.5 years). Extrapersonal symptoms were most common in the study by Lanska et al.[5] as well, with 75% of patients having type B. Type A was uncommon (only 9%). Patients from the study by Weidenfeld et al.[9] were generally in good health. In most of their patients, symptoms of AWS and AWLS ceased within several weeks of diagnosis (seven of nine, 78%). In our study, 60% of the patients' symptoms terminated before or subsequently after diagnosis. There was a recurrence of symptoms after 1 year in two of nine patients (22%) in the report by Weidenfeld et al., but in our study six of 15 patients (40%) still had symptoms at the time of the interview. One of the patients from the Weidenfeld et al. series had a father who claimed to have experienced similar AWS or AWLS symptoms as a child. Five of the nine patients had a family history of migraine or epilepsy. There were also more boys than girls, similar to our study.

The limitations of our study include incomplete enrollment of eligible patients or their families in the prospective or interview portion of the study, so it is possible that any conclusions drawn from this portion of the study are inaccurate. Additionally, the parents were

usually interviewed, and some children may not have reported continued symptoms to the interviewed parent. There was likely a small referral bias. At our institution, however, pediatric neurologists, pediatric ophthalmologists, and pediatricians have ready access to a pediatric neuro-ophthalmologist and have a low threshold for referring children with neuro-ophthalmic problems, even when the diagnosis is readily apparent. Therefore referral bias is minimized, although it cannot be excluded. In addition, patients with AWS or AWLS due to a cerebral neoplasm or epilepsy may not have been referred to our practice, and this bias would also have influenced our results.

In conclusion, AWS and AWLS typically affect young children, and the most common visual complaints are micropsia and teleopsia. The most common associated condition is infection, but half of cases have no obvious etiology. Usually symptoms of AWS and AWLS stop eventually, but in more than one third of the cases, they continue. One quarter of patients without a history of migraine may subsequently develop migraine. The results of our study should be helpful to families of young children and their physicians hoping to provide them with diagnostic and prognostic information regarding this unusual condition.

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A girl, aged 18 was born of parents who were first cousins. She had atypical retinitis pigmentosa with involvement of the macula. The neurological examination showed diffuse disease of the central nervous system, as seen in Friedreich's ataxia. An additional finding … was that of a malformation of the red blood-cells. These cells had a peculiar crenated appearance, due to the appearance of pseudopods or protoplasmic projections.

Frank A. Bassen
Abraham L. Kornzweig
Description of abetaliproteinemia, 1950