

AIWS: Introduction, Overview and Literature Review

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Abstract- With the scope of medical research expanding on a daily basis and with more and more diseases being much better understood than they were even only a few decades ago, we thought it would only be logical if we were to explore those diseases, syndromes and states which have yet to receive their fair share of this ever expanding research paradise we are all currently experiencing. With that being said, our infrequently studied syndrome for today is AIWS (Alice in Wonderland Syndrome). As far as we know, the true first description of the syndrome was in 1952 by Lippman^[1]. First termed by Todd^[2] over 6 decades ago, we have come a long way in understanding the disease since Todd's efforts for which we will be forever thankful. You have probably come across Charles Lutwidge Dodgson's (under the pseudonym Lewis Carroll) "Alice's Adventures in Wonderland" (1865). In the novel, Alice changes in size every once in a while^[3]. The author (Lewis Carroll) did suffer some of the symptoms of this syndrome, such as complex partial seizures and migraine headaches, this has led to some scholars believing that there is a possibility that the author himself may have experienced AIWS^[6,20]. Given his major role in our advancement in knowledge of this syndrome, some refer to it as Todd's syndrome^[4]. Some also refer to it as Lilliputian sight^[6,21]. Here, we will be discussing the syndrome in further detail in an attempt to further understand what patients experience and thereby incentivize ourselves and others to better explore infrequently studied diseases much more often. Four principle visual illusions are usually associated with AIWS, these are: macropsia, micropsia, pelopsia and teleopsia^[4] (we will be defining them later on).

Purpose: To increase knowledge about AIWS and bring it to light.

Index Terms- AIWS, Alice in Wonderland Syndrome, THE SYNDROME OF ALICE IN WONDERLAND, infrequently studied diseases, neuropsychiatry, syndromes, neurology, psychiatry, diseases of perception, HPPD, Napata College, Sudan.

I. INTRODUCTION + CLINICAL SYMPTOMS

With knowledge becoming the true measure of success in the medical field, we have reached levels which were only imaginable a mere few decades ago. With that being said, we have discovered diseases, treated others, developed immunizations and much, much more. Technological advancements (such as the internet) have aided those in developing countries to have a voice in these developments and to keep up with their peers all around the globe. As aforementioned, AIWS is characterized by 4 major visual illusions^[4], they are:

- 1) The perception of objects as being larger than their true size (macropsia)
- 2) The perception of objects as being smaller than their true size (micropsia)
- 3) The perception of objects as being nearer in distance than they truly are (pelopsia) and
- 4) The perception of objects as being further away in distance than they truly are (teleopsia).

Of the intriguing aspects of these symptoms is that they have been reported when observing humans, non-humans, still objects and even moving objects^[4,5]. The array of symptoms is also believed to include^[6]:

- 1) Sense of passage of time
- 2) Zooming of the environment
- 3) Distortion of body image and
- 4) Shape of objects (meta-morphopsia)

Approximately speaking, 30% of adolescents have reported non-clinical symptoms of AIWS^[32]. There is also evidence that visual concentration on a certain object (for seconds to minutes), metamorphopsias start to take place^[32,35,36]. This has been described as a sign of cerebral asthenopia^[32,36,37]. Asthenopia is the abnormal "exhaustion" of the perceptual system.

II. WHAT CAUSES AIWS?

Many medical conditions have been associated with AIWS, some of these include:

- 1) EBV & Infectious mononucleosis^[6,4,10]
- 2) Complex partial epilepsy^[6,22,23]
- 3) Migraine^[7,4,8]
- 4) Nonspecific hyperpyrexia^[7], Malaria^[25]
- 5) Migraine's aura^[9,4]
- 6) Frontal lobe epilepsy^[4,11]
- 7) HPPD^[4]
- 8) Depression^[6]
- 9) Cerebrovascular disease

According to reports, EBV causes neurological symptoms almost exclusively during active infection. Active infections of EBV were diagnosed in patients being tormented by cranial neuritis and cerebellitis, AIWS, facial nerve palsy, progressive macrocephaly as well as lengthened encephalitic illness. Infections of HBV result in adverse neurological outcomes in a substantial number of children, thereby leading to grave long-term complications, as well as the possibility that it could play a role to

the pathogenesis of hippocampal lesions [4,24]. EBV causes infectious mononucleosis.

In the novel, Alice “floats about”, which is a common illusion in complex partial seizures and yet one more reason to believe that the author did actually suffer from AIWS. The author also describes falling down a rabbit hole and a sensation of changing size are directly related to seizure experiences. “AIWS incorporating distortions in body image and shape, often with an impaired perception of time and place, is also associated with that type of epilepsy” [3,26,27].

Medical literature proposes the possibility of fever being a cause of AIWS [7,25]. Even though there is reason to believe that malaria could cause AIWS, there is still uncertainty on whether the malaria itself is the cause or it is the associated hyperpyrexia [7,25]. There is also reason to believe that mefloquine and topiramate possess the possibility to spark symptoms of AIWS [25].

The array of symptoms is followed by an aura in patients who suffer from migraine with aura (constituting approximately 15% of migraineurs). Some of the aural include [6,28]:

- perception of flashing lights that begin in the center of vision and expand in jagged patterns out into the periphery.
- Somatosensory symptoms, examples include: numbness and tingling.
- AIWS

Nuclear medicine techniques are able to demonstrate changes in cerebral perfusion and is used to detect abnormal cerebral areas in patients with classic migraine [29,30], who are tormented by perfusion alterations in either the retina or the visual pathway. “While patients with AIWS, showed abnormal perfusion in medial temporal, hippocampus, temporo-occipital or temporo-parieto-occipital regions” [6,28].

HPPD is a state in which the hallucinogenic effect of a certain drug (in this case LSD) is experienced by the drug user even though they abstained from said drug. To the extent of our knowledge, there has been only one report on a case of AIWS associated with HPPD [4]. According to the DSM-5, “HPPD may recapitulate the prior substance intoxication, reflecting the primary perceptual experience, i.e., visual imagery experienced under hallucinogen intoxication should be re-experienced during HPPD” [4,12]. Extensive reviews on literature regarding HPPD has been previously undergone [4,13]. Even though there have been many attempts at understanding the mechanisms by which LSD intoxication results in the experiences it results in, we have yet to come to a truly deep, comprehensive understanding of how it occurs, a significant proportion of this work is attributed to Lerner AG [4,14,15,16]. There is reason to believe that LSD intake might result in interim finite and capricious damage of the LGN causing maladjustment of the parvocellular cells which could possibly deflect the acuity of forms and shapes, and magnocellular cells which may deflect the acuity of movement of still objects [4,16,17,18,19]. This presentation could easily be confused with psychosis or drug intoxication [6]. A Japanese study once stated that there might be a possibility the ingredients found in cough

syrup could cause AIWS, further studies, however, need to be undertaken to either validate or disprove these findings [6,21]. It is important that we note that the eyes do not suffer from any problem, it is only the brain’s perception that is flawed, what is interesting and aids in this conclusion is that the hallucinations continue on even after the eyes are closed, thereby affirming the conclusion of the flaw being of perception and not of sight [6,21].

This (depression) theory of causation is principally related to the reported case of a 54-year old Japanese businessman who had exhibited AIWS and went on to develop a depressive disorder. There were no abnormal physical findings in the patient. Authors thereby concluded that depressive illness could possibly have played a role in causing AIWS [6,31].

Cerebrovascular disease could, and does, present with a vast array of signs and symptoms which could prove challenging to understand to both the physician and the patient. In 2 reported cases, AIWS was caused by epileptic activity which, in and of itself, was secondary to either hemorrhagic or ischemic lesions, in both cases, however, the lesions affected the occipital lobe of the brain [43] (which is probably why they experienced the visual signs and symptoms of AIWS).

The causes of AIWS have been categorized, by Blom [32], into 8, these are:

- 1) Infectious diseases
- 2) CNS lesions
- 3) PNS lesions
- 4) Paroxysmal neurologic disorders
- 5) Psychiatric disorders
- 6) Medication
- 7) Substance-induced (HPPD)
- 8) Miscellaneous

Some professionals expect the list of vast array of conditions occurring with AIWS to only keep growing with time with the publication of more case reports and case series [32].

III. DURATION OF AIWS AND OUTCOME(S)

For the most part, the duration of AIWS symptoms seems to be relatively short (ranging mostly from minutes to days) [32,33]. With that being said, there are occurrences in which the symptoms lasted for years [32,34] and sometimes for life [32,35].

IV. EPIDEMIOLOGY

We were unable to come across data on AIWS at large, however it is generally assumed that AIWS is rare, some clinical studies amongst patients with migraine present reason to believe that the prevalence rate in this group of patients could be around the 15% range [32,38,39].

V. DIAGNOSIS

With the absence of AIWS in major classifications such as the ICD-10 [32,40] and the DSM-5 [32,12], diagnosis of AIWS is a combination of sound knowledge of the syndrome, its causes, a

thorough neurological examination and proper history taking. Generally speaking, nuclear medicine is of good aid to clinicians when diagnosing AIWS. A functional MRI of a 13-year old conducted by Love et. al showed evidence of lessened activity in both the primary and extrastriate visual cortical regions, the child's MRI also showed "increased activation in parietal lobe cortical regions as compared to a matched control participant" [41]. We were unable to come across studies in which a CT scan was used in diagnosis of AIWS. Even though odds are not in the favor of any significant positive findings (e.g. lesions), cases in which the practitioner suspects central origins should be efficient to initiate auxiliary investigations (e.g. blood tests, brain MRI, EEG, etc.) [32,42]. If the cause were cerebrovascular disease, a CT scan and/or a transcranial Doppler echo study might prove useful. Results associated with the aforementioned will differ depending on the exact cause of AIWS. So far, it is mostly dependent on the practitioner's knowledge, judgement and experience.

VI. TREATMENT

The treatment seems to be depending on that of the underlying cause, a lot of times reassurance alone might be enough [32]. Of course, for the curative process to be the best it can be, it is vital that the clinician is aware of AIWS – that is: its presenting signs, symptoms, possible underlying conditions, treatment to said conditions and the side effects of these treatments. Usually, AIWS occurs with the active phase of the underlying condition which caused it to occur in the first place [32]. It is also of significant importance that the clinician is preforms a careful assessment and is able to judge when it might be at everyone's interest for the patient to be admitted to a healthcare facility.

VII. CONCLUSIONS

Even though it has been over 6 decades since the syndrome has been named, it is only recently that we have begun to truly give AIWS the attention it deserves. This is believed to be the result of multiple factors including our advancements in functional imaging of the brain (i.e. it is believed to have "re-sparked" our interest). However, we have yet to reach levels of understanding that will fulfill our curiosity [32]. We believe it is only a matter of time before we reach higher understandings of this syndrome. All in all, we have made advancements and the syndrome is starting to receive its fair share of medical attention. Unfortunately, we were unable to come across any articles of any type on AIWS in Sudan, so, as far as we know, this is the first article out of Sudan discussing AIWS. We hope it is informative and that it brings light to such syndromes as well as increases the quality and quantity of research coming from our nation and the world. If one thing is for sure, it is that we wish for more attention from the medical research community on this topic as well as other infrequently studied topics. Unfortunately, we believe our understanding of the mind, how it functions, what drugs do to it and how to repair damage done to it is still, at best, at its primary stages, we believe that the advancements in technology will significantly aid in increasing the pace at which we have been studying the mind. This is not to say that we are doing poorly, but rather to motivate ourselves and others to truly "give in 100% and nothing else".

Abbreviations used:

- 1) AIWS = Alice in Wonderland Syndrome
- 2) HPPD = Hallucinogen Persisting Perception Disorder
- 3) EBV = Epstein-Barr Virus
- 4) PNS = Peripheral Nervous System
- 5) CNS = Central Nervous System
- 6) ICD-10 = The International Classification of Diseases, 10th Revision
- 7) DSM = Diagnostic and Statistical Manual of Mental Disorders
- 8) LSD = Lysergic Acid Diethylamide
- 9) LGN = Lateral Geniculate Nucleus
- 10) MRI = Magnetic Resonance Imaging
- 11) CT = Computed Tomography

Guide

Author; Year; *Title*; Journal

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