

Alice in Wonderland Syndrome...the Iceberg

HAMA University First International Medical Conference, May 7-9, 2017

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Key words: Alice, disorientation, perception, and infectious mononucleosis.

1. Abstract:

Alice in Wonderland Syndrome is a rare and important syndrome in childhood. It is a disorienting neurological condition that affects perception. The patient experience size distortion such as micropsia, macropsia, pelopsia, or teleopsia. Size distortion may occur of other sensory modalities.

This syndrome has many different etiologies; however EBV infection is the most common cause in children, while migraine affects more commonly adults. Some dangerous cases like Brain tumors, and some physiologic states as sleep onset and lack of sleep can cause AIWS as well. The use of psychiatric drugs can be another reason for this syndrome. AIWS can be caused by abnormal electrical activity in the brain causing abnormal blood flow in the cerebral parts that process visual perception and other sensations.

2. Background:

Alice in Wonderland syndrome is named after Lewis Carroll's famous 19th century novel Alice's Adventures in Wonderland. In the story, the title character, Alice, experiences numerous situations similar to those of micropsia and macropsia. Speculation has arisen that Carroll may have written the story using his own direct experience with episodes of micropsia resulting from the numerous migraines or possible temporal lobe epilepsy he may have suffered from. AIWS is a well-known example of the Art-Disease Relationship.

3. Name synonyms:

Todd's syndrome. The syndrome is sometimes called Todd's syndrome, in reference to an influential description of the condition in 1955 by Dr. John Todd (1914-1987), who was a British Consultant Psychiatrist at High Royds Hospital at Menston in West Yorkshire. Todd discovered that several of his patients experienced severe migraine headaches causing them to see and perceive objects as greatly out of proportion. They have altered sense of time and touch, as well as distorted perceptions of their own body.

4. pathophysiology:

To date, only a few studies regarding AIWS reported neuroimaging evidences of damage at the level of cerebral cortices. A critical area for developing AIWS seems to be the carrefour of three major areas, the TPO-C, which is the crossroad of temporooccipital, parietooccipital, and temporoparietal junctions (TOJ, POJ, and TPJ). TPO-C is where visual and somatosensory information are integrated to generate the inner and external representation of self. This seems to be supported by several reports in which anatomical lesions of patients experiencing AIWS were located in right or left TPO-C. The spectrum of symptoms appears to be wider and more complex if lesions involve more anterior regions of the brain. In fact, theoretically, if a lesion is located in occipital regions we observe more likely simple visual disturbances, while if the lesion is closer to parietal and temporal areas also somatosensory and cognitive disorders will combine with the visual ones, resulting in more complex symptoms, as in an integration abnormality.

The connections between visual, parietal, and temporal cortices in the image- and non-image-forming visual system may be more complex than expected and, in some cases, it may pass through the thalamus. The data by Imbert and Bignall showed that visual stimulation can activate the orbitofrontal cortices without activating the somatosensory cortex in a model of thalamectomized cat. It suggests that a relevant part of projections from the occipital cortex passes through the thalamus to be conveyed to the somatosensory cortex. Interestingly, in this study, the lateral geniculate nucleus was intact, showing that it is not an obligatory relay for visuosomatosensory connections. In support of these data, in a recent case of facial blind sight, some connections between the lateral fusiform gyrus and thalamic nuclei have been implicated in unconscious residual visual faculties of the subjects

5. Causes:

The following summarizes AIWS etiologies reported in literature. More Common Causes Reported of AIWS:

Headaches: (i) Migraine (ii) Abdominal migraine (iii) Cluster headache (iv) Tension type headache (v) HANDEL: syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis.

Epilepsy: (i) Temporal lobe epilepsy (ii) Frontal lobe epilepsy.

Infectious diseases: (i) Epstein-Barr virus (ii) Coxsackie B1 virus (iii) Cytomegalovirus (iv) Influenza A virus (v) Mycoplasma (vi) Varicella-zoster (vii) Typhoid encephalopathy (viii) Lyme neuroborreliosis (ix) Streptococcus pyogenes (scarlet fever and tonsillopharyngitis) (x) Parainfective vasculitis.

Cerebrovascular diseases: (i) Intraparenchymal hemorrhagic stroke (ii) Ischemic stroke (iii) Cavernous angioma (iv) Robin Hood syndrome (v) Pituitary infarction.

Other organic brain diseases: (i) Acute disseminated encephalomyelitis (ii) Glioblastoma.

Psychiatric disorders: (i) Depressive disorder (ii) Cotard Syndrome (iii) Capgras Syndrome (iv) Schizophrenia (v) Schizoaffective disorder.

Drugs: (i) Dextromethorphan (ii) Cough syrup (containing dihydrocodeine and DL methylephedrine) (iii) Montelukast (iv) Topiramate (v) LSD (vi) Hallucinogen Persisting Perception Disorder (HPPD) after LSD withdrawal (vii) Toluene-based solvent.

Out of 166 cases of AIWS published, the most common cause is migraine (27.1%), followed by infections (22.9%), principally EBV (15.7%). In decreasing order, other etiologies are as follows: brain lesions (7.8%), medication (6%) and drugs (6%), psychiatric disorders (3.6%), epilepsy (3%), disease of the peripheral nervous system (1.2%), and others (3%). In about 20% of patients no cause of AIWS was found. In 65% of cases AIWS occurred in children under 18 years of age.

-EBV Infections mainly Infectious Mononucleosis: Infectious mononucleosis (IM), also known as mono, kissing disease, or glandular fever, is an infection commonly caused by the Epstein-Barr virus (EBV). Most people are infected by the virus as children, when the disease produces little or no symptoms. In young adults, the disease often results in fever, sore throat, enlarged lymph nodes in the neck, and tiredness. Most people get better in two to four weeks; however, feeling tired may last for months. The liver or spleen may also become swollen. In less than one percent of cases splenic rupture may occur.

-Migraines: Migraine is a primary headache disorder characterized by recurrent headaches that are moderate to severe. Typically, the headaches affect one half of the head, are pulsating in nature, and last from two to 72 hours. Associated symptoms may include nausea, vomiting, and sensitivity to light, sound, or smell. The pain is generally made worse by physical activity. Up to one-third of people have an aura: typically a short period of visual disturbance which signals that the headache will soon occur. Occasionally, an aura can occur with little or no headache following it.

-Brain tumors: A brain tumor or intracranial neoplasm occurs when abnormal cells form within the brain. There are two main types of tumors: malignant or cancerous tumors and benign tumors. Cancerous tumors can be divided into primary tumors that start within the brain, and secondary tumors that have spread from somewhere else, known as brain metastasis tumors. All types of brain tumors may produce symptoms that vary depending on the part of the brain involved. These symptoms may include headaches, seizures, problem with vision, vomiting, and mental changes. The headache is classically worse in the morning and goes away with vomiting. More specific problems may include difficulty in walking, speaking, and with sensation. As the disease progresses unconsciousness may occur.

-Sleep related conditions especially sleep onset, and lack of sleep: Sleep onset is the transition from wakefulness into sleep. Sleep onset usually transmits into non-rapid eye movement sleep (NREM sleep) but under certain circumstances (e.g. narcolepsy) it is possible to transit from wakefulness directly into rapid eye movement sleep (REM sleep). Sleep deprivation is the condition of not having enough sleep; it can be either chronic or acute. A chronic sleep-restricted state can cause fatigue, daytime sleepiness, clumsiness and weight loss or weight gain. It adversely affects

the brain and cognitive function. However, in a subset of cases sleep deprivation can, paradoxically, lead to increased energy and alertness and enhanced mood; it has even been used as a treatment for depression.

-Psychiatric medications: A psychiatric medication is a licensed psychoactive drug taken to exert an effect on the chemical makeup of the brain and nervous system. Thus, these medications are used to treat mental illnesses. Usually prescribed in psychiatric settings, these medications are typically made of synthetic chemical compounds. Since the mid-20th century, such medications have been leading treatments for a broad range of mental disorders and have decreased the need for long-term hospitalization, therefore lowering the cost of mental health care.

-Addictions: Addiction is a brain disorder characterized by compulsive engagement in rewarding stimuli, despite adverse consequences. Despite the involvement of a number of psychosocial factors, a biological process – one which is induced by repeated exposure to an addictive stimulus – is the core pathology that drives the development and maintenance of an addiction. The two properties that characterize all addictive stimuli are that they are reinforcing (i.e., they increase the likelihood that a person will seek repeated exposure to them) and intrinsically rewarding (i.e., they are perceived as being inherently positive, desirable, and pleasurable).

6. Epidemiology:

The exact prevalence of the AIWS is unknown, for several reasons. First, no epidemiologic studies on large scale are available. Second, the lack of univocally accepted diagnostic criteria for AIWS casts a shadow on reported data that should then be considered carefully.

A study conducted on 3224 Japanese adolescents, aged 13 to 18 years, demonstrated that the occurrence of micropsia and macropsia was 6.5% in boys and 7.3% in girls, suggesting that the visual illusions of AIWS may be not so rare in general population.

The average age of the start of Alice in Wonderland syndrome is six but it is very normal for some to experience the syndrome from childhood to their late 20s. However, some still have problems in their 70s.

7. Sex:

The male/female ratio seems to vary with the age: while in younger age male are predominantly affected with 2.69-fold risk of having AIWS (in a sample aged 5 to 14 years), no significant differences in sex prevalence were recorded in junior students (13–15 years old) by Abe et al. , while females were significantly more prevalent (56.7%) among senior students (16–18 years).

8. Signs and symptoms:

AIWS affects the sense of vision, sensation, touch, and hearing, as well as one's own body image. A prominent and often disturbing symptom are experiences of altered body image. The people may find that they are confused as to the size and shape of parts of (or all of) their body. They may feel as though their body is expanding or getting smaller. AIWS also involves perceptual distortions of the size or shape of objects.

Patients with certain neurological cases have experienced similar visual hallucinations "Lilliputian," which means that objects appear either smaller or larger than they actually are. Some may experience attacks of migrainous headache associated with eye redness, flashes of lights and a feeling of giddiness.

Patients may experience either micropsia or macropsia. Micropsia is an abnormal visual condition, usually occurring in the context of visual hallucination, in which affected persons see objects as being smaller than those objects actually are. Macropsia is a condition where the individual sees everything larger than it actually is.

Some people feel that objects appear small and distant (teliopsia) or large and close (peliopsia). Others feel that leg or arm is swinging. Some people hear the voices of people quite loud and close or faint and far.

The eyes themselves are normal, but the person will often 'see' objects as the incorrect size, shape or perspective angle. Therefore, people, cars, buildings, houses, animals, trees, environments,

etc., look smaller or larger than they should be, or that distances look incorrect; for example a wall may appear to be very huge, or the ceiling may appear too close or so far.

The affected person may also lose the sense of time, a problem similar to the lack of spatial perspective. In other words, time seems to pass very slowly. The lack of time, and space, perspective leads to a distorted sense of velocity. This can then cause the person to feel as if movement, even within his or her own home, is strange, futile, or difficult.

Some people may have fever due to causative reasons or unrelated cases, and with a high fever, they may experience more intense and overt hallucinations, seeing things that are not there and misinterpreting events and situations.

Other less common symptoms may include loss of limb control and general dis-coordination, memory loss, lingering touch and sound sensations, and emotional experiences.

9. Diagnosis:

The diagnosis can be presumed when other causes have been ruled out and if the patient presents symptoms along with migraines and complains of onset during the day (although it can also occur at night).

10. Differential Diagnosis:

It is very important (especially in our community) not to accuse the person especially the child one that he or she is lying.

-Charles Bonnet syndrome: Visual release hallucinations, also known as Charles Bonnet syndrome (CBS), is the experience of complex visual hallucinations in a person with partial or severe blindness. First described by Charles Bonnet in 1760, it was first introduced into English-speaking psychiatry in 1982.

-Visual and Eye 's disturbances.

-Intoxications: toxicity is the degree to which a substance can damage an organism. Toxicity can refer to the effect on a whole organism, as well as the effect on a substructure of the organism, such as a cell (cytotoxicity) or an organ such as the liver (hepatotoxicity). Sometimes the word is more or less synonymous with poisoning in everyday usage. A central concept of toxicology is that the effects of a toxin are dose-dependent; even water can lead to water intoxication when taken in too high a dose, whereas for even a very toxic substance such as snake venom there is a dose below which there is no detectable toxic effect.

-Drugs abuse and addictions: Substance abuse, also known as drug abuse, is a patterned use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others, and is a form of substance-related disorder. Widely differing definitions of drug abuse are used in public health, medical and criminal justice contexts. In some cases criminal or anti-social behavior occurs when the person is under the influence of a drug, and long term personality changes in individuals may occur as well. In addition to possible physical, social, and psychological harm, use of some drugs may also lead to criminal penalties, although these vary widely depending on the local jurisdiction. Drugs most often associated with this term include: alcohol, barbiturates, benzodiazepines, cannabis, cocaine, methaqualone, opioids and substituted amphetamines. The exact cause of substance abuse is not clear, with theories including one of two: either a genetic disposition which is learned from others, or a habit which if addiction develops, it manifests itself as a chronic debilitating disease.

-Hysteria: Hysteria, in the colloquial use of the term, means ungovernable emotional excess. Generally, modern medical professionals have abandoned using the term "hysteria" to denote a diagnostic category, replacing it with more precisely defined categories, such as somatization disorder. In 1980, the American Psychiatric Association officially changed the diagnosis of "hysterical neurosis, conversion type" (the most extreme and effective type) to "conversion disorder".

11. Lab Studies:

CBC, LDH, CRP, ESR, Mono test, etc.

12. Imaging Studies:

Chest X Ray, Brain CT or MRI, etc.

13. Consultations:

We may need multidisciplinary approach. The subspecialty team includes Pediatric, neurologic, ophthalmologic, psychiatric, social, surgical, and other ones.

14. Prognosis:

The long term prognosis is depending on the etiologic cause. In regarding to short term prognosis, the bodily related distortions can recur several times a day and may take some time to abate. Understandably, the person can become alarmed, frightened, and panic-stricken throughout the course of the hallucinations—maybe even hurt themselves or others around them. The symptoms of the syndrome themselves are not harmful and are likely to disappear with time.

15. conclusion:

AIWS is still poorly known and probably misdiagnosed for the lack of clear and universally accepted diagnostic criteria. We should do our best to do a right causative diagnosis as soon as possible. Early diagnosis may give very valuable help for the patient and for the doctor as well. Be careful that child's lying is not a good diagnosis at all.

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