# KYOVR
# DeafBlind Conference

November 20, 2019

Presenter: Mark Poston, M.A.

# Overview of Usher Syndrome and Psychiatric Conditions Associated with the Syndrome

# Definitions/Classification

- DeafBlind definition
  - Congenitally Deaf/HoH, Adventitiously Blind
  - Congenitally Blind, Adventitiously Deaf/HoH
  - Congenitally DeafBlind
  - Adventitiously DeafBlind

# Learning Objectives

- Participants will identify distinguishing clinical features associated with the 3 types of Usher Syndrome
- Participants will gain an understanding of etiological factors and the diagnostic process associated with Usher Syndrome
- Participants will become familiar with mental health conditions and symptoms sometimes occurring with Usher Syndrome.

# DeafBlindness: Causes

- Multiple Congenital Anomalies
  - Hydrocephaly
  - Microcephaly
  - Fetal Alcohol Syndrome
  - Maternal Drug Abuse
- Prematurity

# DeafBlindness: Causes

- Prenatal Infections
  - Syphilis
  - Toxoplasmosis
  - Rubella
  - CMV
  - Herpes
  - AIDS

# DeafBlindness: Causes

- Post-natal Causes
  - Asphyxia
  - Head Injury
  - Stroke
  - Encephalitis
  - Meningitis
  - Tumors
  - Metabolic Disorders

# DeafBlindness: Causes

- Psychogenic Causes
  - Conversion Disorder
- Genetic Syndromes
  - CHARGE
  - Down's Syndrome
  - Trisomy 13
  - Usher Syndrome

# Usher Syndrome

- Genetic condition (autosomal recessive)
  - Sensorineural hearing loss
  - Retinitis pigmentosa (RP)
  - Balance issues
  - Most frequent cause of deaf-blindness
  - Estimates are 1 in 10 carry some form of the recessive gene
  - There are at least 10 genes that cause Usher Syndrome
  - There are 3 types and 9 subtypes of Usher Syndrome
  - Both parents must have the same recessive gene in order to have an affected offspring (25% chance for each child)
  - If the genes are different, the offspring will be carriers of the recessive gene but not be affected
  - Prevalence is 5-6 per 100,000 in the USA

# Usher Syndrome Type Distinction

- Severity of hearing loss
- Presence of absence of vestibular function
- Onset of vision loss

- All variables must be considered in making the diagnosis as hearing loss alone is insufficient to determine whether Usher Syndrome is present or to distinguish between the subtypes

# Type I Usher Syndrome

- Congenital profound sensorineural hearing loss
- No vestibular function (vestibular areflexia)
  - Developmental delays in sitting and walking
- Night blindness apparent during the 1st decade of life
  - Child may be afraid of the dark
  - Often described as clumsy or accident prone because they bump into and/or trip over things or people
- Deterioration of visual field and acuity begins between the second and third decade of life
- Cataracts are common
- Second grief cycle typical for family upon discovering child will eventually be blind
- Sign language is the primary mode of communication

# Type II Usher Syndrome

- Mild to severe sensorineural hearing loss (often considered hard of hearing)
- Vestibular function is typically normal
- Onset of night blindness during second decade of life
- Acuity and visual field loss is less severe than with Type 1 during the third and fourth decades of life
- Subjective sense of progressive hearing loss due to decreasing visual cues
- Amplification and lip-reading typically sufficient for effective communication

# Type III Usher Syndrome

- Hearing loss is progressive
- Hearing loss is moderate sloping to profound during the first decade of life
- By the fourth decade of life, hearing loss is profound
- May or may not have vestibular function issues
- Rare in the USA

# Retinitis Pigmentosa (RP)

- The vision loss associated with Usher's Syndrome is RP
- Degenerative disease of the retina due to a genetic malformation or absence of one or more proteins necessary for retinal survival
- Progressive visual loss leading to blindness
- First symptom is typically difficulty seeing at night or night blindness as the rods (photoreceptor) begin to die
- Loss of peripheral (side) vision comes later as cones (photoreceptor) begin to die.  Fine detail and color also affected.
- Vision loss is so gradual as to often hardly be noticed as people naturally adapt

# Retinitis Pigmentosa

- Many people with Usher Syndrome retain pin hole vision into the middle decades of life
- It is reported that 51% of individuals with Type I and 72% with Type II retain visual acuity of 20/40 or better in a small visual field in one or perhaps both eyes.

# Diagnosis of Usher Syndrome

- A combination of audiologist and ophthalmologist is sufficient to make the diagnosis.

- To diagnose hearing loss, the audiologist has a number of measures that can be used. Some tests are better than others. The definitive measure is the Auditory Brainstem Response (ABR). For this test, electrodes are placed on the individual's head and brainwave activity is measured in response to sound. Another excellent measure is the Otoacoustic Emissions (OAE) which checks the inner ear response to sound. As with the ABR, this test does not rely on an individual's behavioral response.

# Diagnosis of Usher Syndrome

- An ophthalmologist has various methods available to measure visual acuity and visual field. Direct observation to evaluate the condition of the retina is one option for determining whether a person has RP. Attenuated blood vessels, waxy pallor, and clumps of dead retinal cells give indication of RP. However, these physical signs do not precede the manifestation of RP symptoms.

- The definitive test for RP is an electroretinogram (ERG). The advantage of this test is it will show abnormality long before signs of cell death on the retina.

- Once an individual is diagnosed with Usher Syndrome, there is genetic testing available to determine the specific genetic type.

# Psychological Factors

- Studies have described the presence of various mental disorders associated with Usher Syndrome.
- Most frequently described are schizophrenia-like or psychotic symptoms.
- Mood and behavioral disorders are rarely reported.

- Question: Is there a mechanism of association between Usher Syndrome and mental or behavioral disorders?  If so, what is this mechanism or mechanisms?

# Psychological Factors

- A 1959 study by Hallgren reported a diagnosis of psychosis in 26 of 114 (23%) individuals with Usher Syndrome.
- A 1970 study by Nuutila found 6 out of 131 (4.5%) individuals with Usher Syndrome to be psychotic.
- Subsequent studies by Dammeyer and then by Grondahl and Mjoen found 1 in 26 (3.84%) and 1 in 27 (3.70%) respectively had a diagnosis of schizophrenia.
- The prevalence of schizophrenia in the US is 1.1%, significantly below what is found with the Usher Syndrome population.
- It should be noted that a diagnosis of psychosis in patients with Usher Syndrome is difficult due to communication barriers.

# Psychological Factors

- So, is there a mechanism of association between Usher Syndrome and mental or behavioral disorders? If so, what is the mechanism or mechanisms?
- The researchers can't agree on the prevalence of psychotic symptoms. Their findings range from 3.7% to 23%. They do agree that psychosis is hard to establish with this population due to communication difficulties.
- Nevertheless, if accurate, the prevalence of schizophrenia is 3 to 4 times higher among those with Usher Syndrome than among the US population.

# Psychological Factors

- Things to consider:
  - Other sources of psychotic (or psychotic – like) symptoms (e.g., hallucinations)
    - Normal hallucinations such a hypnagogic and hypnapompic
    - Brain tumors
    - Depression/mood disorders
    - PTSD flashbacks/intrusions
    - Chemical induced (drugs, toxins)
    - Lewy Body Dementia
    - Delirium
    - Dissociation
    - Migraines
    - Parkinson's
    - Sleep deprived hallucinations
    - Stress and social isolation
    - Sensory deprivation
    - Charles Bonnet Syndrome

# Psychological Factors

- Things to consider:
  - Usher Syndrome and the Central Nervous System (CNS)
    - CT and MRI studies have shown various abnormalities of the CNS with people who have Usher Syndrome.
      - Cerebellar and cerebral atrophy, focal lesions, hypoplasia of corpus callosum, dilation of the 4$^{th}$ ventricle, decrease in cranial volume with an increase in the subarachnoid spaces, arachnoid cyst
      - These abnormalities are reported both in Usher Type I (88.9%) and Type II (66.7%). Usher Type I patients were more severely affected with more prominent atrophy and cerebellar involvement (60% presented cerebellar abnormality).
      - The most common abnormal pattern (nearly half the patients) was atrophy involving mainly the vermis. Although abnormal gate was very common in both Usher Type I (89.9%) and Type II (66.7%) patients, no correlation between cerebellar and gate abnormalities was found. According to the authors the pathogenesis of gait seems to be related to the loss of vestibular function in Usher I and to cerebellar structural abnormalities in Usher II.

# Psychological Factors

- Psychotic Disorders
  - There are limited reports that offer a description of psychotic features of Usher patients.  Often the descriptions of auditory and visual hallucinations are only presumptive and based on the behavior of the patients due to communication barriers.
  - Sometimes the diagnosis of schizophrenia cannot be established with certainty
  - Psychometric evaluation cannot be performed in most cases.

# Psychological Factors

- Persecutory delusions were the most common form of delusion reported. Religious delusions were noted in a couple of cases. In most cases, the authors reported a clinical picture resembling paranoid schizophrenia. No catatonic symptoms were observed. Aggressive behavior was noted in the majority of cases. Patients were often noted to be anxious and irritable.

- Mood and Behavior Disorders
  - There were very few case studies that described clinical manifestations of mood and behavioral disorders in Usher patients. There were some cases reported of Usher subjects having ADHD, panic attacks, anxiety, depression and obsessive rituals with psychotic manifestations. Learning disabilities were often suspected as well.

# Psychological Factors

- Is there a mechanism of association between Usher Syndrome and psychiatric issues?

- Although a significant number of Usher patients suffer from psychiatric symptoms, the mechanism of association is unclear.  In general, three theories have been proposed:

  - Genetic hypothesis
  - Neurological compromise
  - Stress-related theories

# Psychological Factors

- Genetics
  - With schizophrenia, various genes are reported as possibly causative. One of these genes is on the same chromosome and in close proximity to the Usher II gene. This would warrant further investigation.

- Central Nervous System (CNS)
  - Usher Syndrome is a complex syndrome with diffuse neurological involvement. Some suggest the aggregate cerebral involvement could explain the multiple or mixed mental and behavioral manifestations such as hallucinations, delusions, ADHD, depression, and why they coexist in the same person. Some authors suggest the CNS findings may be the consequence of effects from the Usher genes.

# Psychological Factors

- Stress-related theory
  - Visual or auditory loss is associated with a higher rate of depression, suicidal behavior, psychological stress and social difficulties.  Chronic stress may be related to a progressive visual loss in an individual who has already experienced deafness and has come to rely on vision as the primary sense organ.

# Conclusion

- The genesis of increased psychotic illness in individuals with Usher Syndrome would appear to be multi-determined. Multiple genes and environmental factors such as isolation, sensory deprivation, anxiety and stress-related issues may be involved.
- The diffuse CNS abnormalities may come as a result of Usher genes. These abnormalities may have contributed to the atypical or mixed psychiatric symptoms reported in Usher patients.
- Further research is needed to confirm these hypotheses, although the association between Usher Syndrome and mental and behavioral disorders cannot be dismissed.