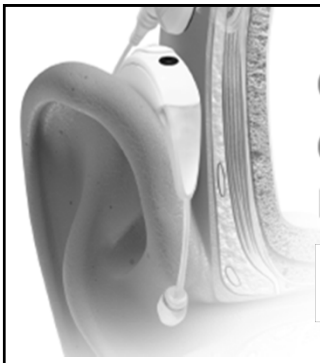
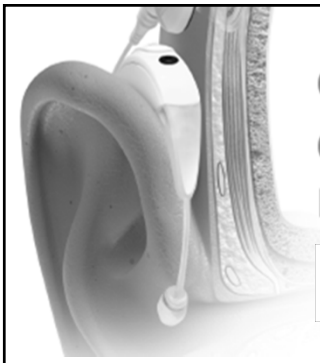


GRAND ROUNDS IN COCHLEAR IMPLANTS

Hosted by Advanced Bionics

Presented by Jolie Fainberg, MA, FAAA
March 27. 2015

Advanced Management of Complex Cases: Usher Syndrome



GRAND ROUNDS IN COCHLEAR IMPLANTS

Hosted by Advanced Bionics

Presented by Jolie Fainberg, MA, FAAA
March 27. 2015

Learner Objectives:

- The participants will be able to identify the three types of Usher Syndrome.
- The participants will be able to describe the clinical features of Usher Syndrome.
- The participants will be able to list the treatment and intervention options for children with Usher Syndrome.

- Need Technical Support? Contact AudiologyOnline at 1-800-753-2150
- You must stay logged in for the duration of this course in order to be eligible to earn CEU credit.
- This course is offered for Continuing Education Units (CEUs) from AudiologyOnline if you are a CEU Total Access member.
- Be sure to take the exam following course completion to earn credit.

Identification and Management of Children with Usher Syndrome

Jolie C Fainberg, MA

Introduction

Usher Syndrome is a rare genetic disorder that is the leading genetic cause of deaf-blindness. It was named for a Scottish Ophthalmologist, Charles Usher, who recognized it as a syndrome through a survey of 69 deaf individuals who also suffered from vision impairment.

Introduction

Dr. Usher described the pathology and transmission of the syndrome in a 1914 paper entitled *On the Inheritance of Retinitis Pigmentosa.* He recognized this syndrome as an inherited disease. Usher's work was a continuation of research on retinitis pigmentosa begun by Albrecht von Graefe and his student Richard Liebreich in the late 1850s.

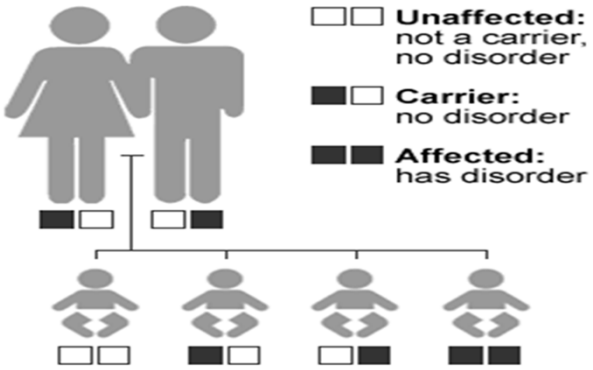
Prevalence

Although Usher Syndrome is rare, with the incident rate worldwide estimated at 1:6,000-20,000, it is devastating for those who are affected by it. Approximately 10% of all children born with congenital, profound sensorineural hearing loss have Usher Syndrome and an estimated 50% of all people who are deaf and blind.

Genetic Features

- Usher Syndrome is caused by an autosomal recessive gene and manifests in three clinical types.
- **Recessive** means that a person must inherit the same gene from each parent in order to have the disorder
- **Carrier** is a person with one affected gene who does not have the disorder, but can pass either the affected or the unaffected gene on to his or her child
- An individual with Usher syndrome usually has inherited the gene from each parent

Genetic Features



1-in-4 chance of having a child with Usher syndrome
2-in-4 chance of having a child who is a carrier
1-in-4 chance of having a child who neither has Usher syndrome nor is a carrier

Poll Question 1

Poll Question 2

Type I

Type I is characterized by severe to profound deafness at birth, delayed development of motor skills, ongoing and often worsening vestibular system and balance issues, and early onset of loss of vision caused by Retinitis Pigmentosa (RP). Type I is further divided into seven distinct subtypes, designated as types IA through IG.

Type I

Usher syndrome Type I is estimated to occur in at least 4 per 100,000 people. It may be more common in certain ethnic populations, such as people with Ashkenazi (central and eastern European) Jewish ancestry and the Acadian population in Louisiana.

Type II

Type II is characterized by mild to severe hearing loss at birth, no balance issues and evidence of loss of sight in teen years because of RP. Usher syndrome type II has at least three described subtypes, designated as types IIA, IIB, and IIC. Type II is thought to be the most common form of Usher syndrome, although the frequency is unknown.

Type III

Type III includes progressive hearing loss, possible vestibular issues, and progressive vision loss through Retinitis Pigmentosa. Type III Usher syndrome is rare and more common in the Finnish population, however, where it accounts for about 40 percent of all cases.

Genetic Features

Gene Type		Clinical Type	Phenotype	
	HEARING		**VISION**	**BALANCE**
USH1B,USH1C, USH1D,USH1F, USH1G, USH1H, USH1J	Born with severe to profound hearing loss.	**Type I**	Progressive vision loss beginning in childhood.	Delayed sitting and walking with ongoing balance issues often becoming more severe as vision deteriorates.
USH2A, USH2C	Born with mild to severe hearing loss with progressive loss into adulthood.	**Type II**	Progressive vision loss beginning in adolescence to early adulthood.	No balance issues.
USH3A, USH3B	Born with normal hearing with progressive hearing loss developing in adolescence to early adulthood.	**Type III**	Progressive vision loss beginning in adolescence to early adulthood.	Varying degrees of balance.

Genetic Features

There are currently 11 genes associated with Usher Syndrome. Each of these known genes, and presumably others not yet recognized, synthesize proteins that play a role in the formation and health of the sensory systems of the ear, eye and vestibular system.

Genetic Features

Usher Type	Human Gene
USH1B	*MYO7A*
USH1C	*USH1C*
USH1D	*CDH23*
USH1E	-
USH1F	*PCDH15*
USH1G	*USH1G*
USH1H	-
USH1J	*CIB2*
USH2A	*USH2A*
USH2C	*GPR98*
USH2D	*CIP98*
USH3A	*CLRN1*
USH3B	*HARS*

Poll Question 3

Diagnosis: Vision

Evaluation of the eyes may include a visual field test to measure a person's peripheral vision, an electroretinogram (ERG) to measure the electrical response of the eye's light-sensitive cells, and a retinal examination to observe the retina and other structures in the back of the eye.

Diagnosis: Hearing

A complete audiologic evaluation should be completed including audiogram, ABR, impedance measures and otoacoustic emissions.

Diagnosis: Vestibular

A complete vestibular evaluation, including electronystagmogram (ENG) which measures involuntary eye movements that could signify a balance problem, is recommended.

Clinical Features

- Vision Loss
- Hearing Loss
- Vestibular Function

Vision Loss

The gradual vision loss in people with Usher Syndrome is caused by Retinitis Pigmentosa or RP which affects the layer of light-sensitive tissue at the back of the eye (the retina). In Usher Syndrome, RP is caused by a mutated gene in the retina which does not produce a protein needed by the rods to survive.

Vision Loss

In early adolescence, Usher Syndrome patients lose their night vision because of the slow destruction of these rods. As the rods die off, peripheral vision begins to narrow leading to tunnel vision in which a person can only see out of the center of the eye. The central vision, which is controlled by the cones, is eventually affected leading to complete blindness.

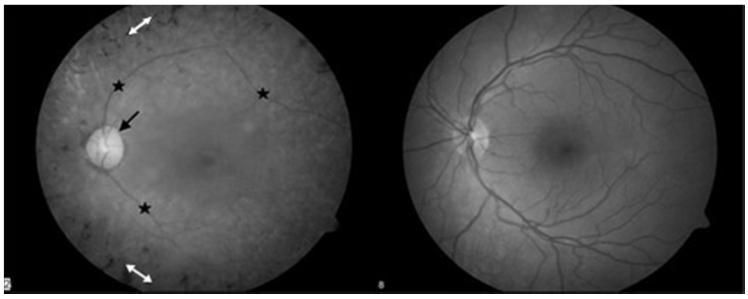
Vision Loss

In Type I USH, night blindness is typically apparent by age 10, so these children are often described as clumsy because they bump into, or trip over, objects. Significant deterioration of visual field and acuity begins between the second and third decade of life, with cataracts being a common complication.

Vision Loss

The regression of RP can occur at different rates in different individuals, but many people with Usher Syndrome are legally blind by early adulthood. Many people with retinitis pigmentosa retain some central vision throughout their lives, however.

Vision Loss



Photograph of the retina of a patient with Usher syndrome (left) compared to a normal retina (right). The optic nerve (arrow) looks very pale, the vessels (stars) are very thin and there is characteristic pigment, called bone spicules (double arrows). Source : NIH

Vision Loss

Research scientists are working to determine ways to slow, stop or even reverse the degeneration of rods and cones, or possibly bypass the rods and cones to maintain vision via retinal implant.

Vision Loss

Gene replacement therapies, gene preservation therapies, drug therapies, induced pluripotent stem cell therapies, optogenetics, and other cutting edge research has brought the development of safe and efficacious treatments closer to restoring hearing, as well as sight, to individuals with Usher Syndrome.

Poll Question 4

Hearing Loss

Type I Usher syndrome presents with congenital, profound sensorineural hearing loss at birth. Because the vision impairment is typically discovered later, the family may experience a second period of grief upon learning that their deaf child will eventually be blind. These children benefit from early bilateral cochlear implantation and auditory-verbal therapy.

Hearing Loss

Type II Usher syndrome exhibits a stable, sloping, moderate-to-severe sensorineural hearing loss and can benefit from amplification. The Subtype IIa, however, may demonstrate progressive loss not found in other Type II expressions. These children may need a CI when the hearing loss becomes severe to profound.

Hearing Loss

Type III Usher syndrome hearing loss is not present at birth but with progressive hearing loss. During the first decade of life, the hearing loss is moderate sloping to profound and progresses to profound by the fourth decade.

Vestibular Dysfunction

Usher Syndrome Type 1 is commonly associated with absent vestibular function, and vestibular dysfunction develops in approximately 50% of those with Usher Syndrome Type III. Recognition of vestibular dysfunction in this population could facilitate earlier diagnosis of Usher Syndrome.

Vestibular Dysfunction

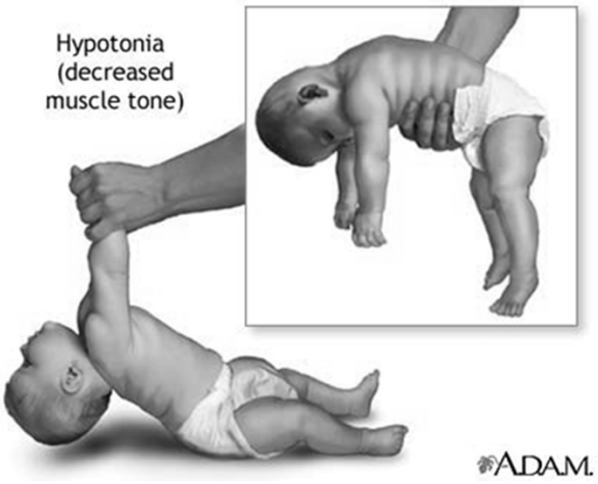
The presence of vestibular dysfunction in a child with profound sensorineural hearing loss could suggest Type I. In fact, 36% of those born with profound deafness and vestibular dysfunction have Usher Syndrome Type I. As other causes of profound deafness with vestibular issues are ruled out, the likelihood rises.

Manifestations of Vestibular Dysfunction

Babies

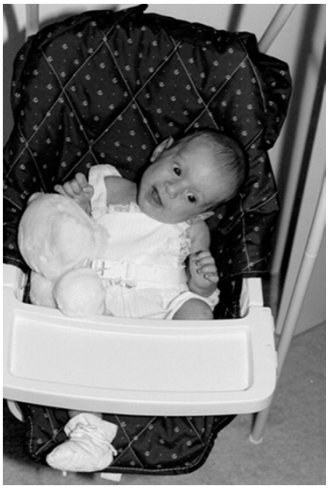
- Head lag – By age 6 weeks, babies with normal vestibular function can hold their heads in line with their bodies when pulled to a sitting position while lying on their backs. The heads of babies with USH1 hang backwards.

Manifestations of Vestibular Dysfunction



Manifestations of Vestibular Dysfunction

- In addition, when held upright, they cannot steady their heads, resulting in an uncontrolled bobbing, and their heads fall to the side when placed in a supported sitting position.



Manifestations of Vestibular Dysfunction

- Arching of their backs when held
- Late sitting – Sitting between ages 9 and 12 months rather than by age 7 months. Tripod sitting until then.

Manifestations of Vestibular Dysfunction

- W-sitting once they do sit

Manifestations of Vestibular Dysfunction

- Late crawling, often starting with a combat crawl

Manifestations of Vestibular Dysfunction

Toddlers

- Late walking, usually at age 18 months or later, and then with poor balance and an awkward gait that remains obvious through preschool age or later.

Manifestations of Vestibular Dysfunction

Preschool and Early Childhood

- Awkward, uncoordinated and clumsy at playground games
- May fall often and easily
- Bumping into furniture
- Losing balance when pushed slightly off their center of gravity

Manifestations of Vestibular Dysfunction

Later Childhood through Adult

- Decreased ability to track two processes at once
- Difficulty in handling sequences
- Decreased mental stamina
- Memory retrieval ability
- Decreased sense of internal certainty
- Decreased ability to grasp the large whole concept

Poll Question 5

Treatment and Intervention Considerations

Currently, there is no cure for Usher syndrome. The best treatment involves early identification and intervention. The exact nature of the intervention will depend on the severity of the hearing and vision loss.

Treatment and Intervention Considerations

In Usher Type II and III, amplification is recommended as soon as the hearing loss is identified. In addition, speech-language or auditory-verbal therapy should be started as soon as the child receives hearing aids. Most of these children will do well with early intervention.

Treatment and Intervention Considerations

For Type I Usher, early, bilateral cochlear implantation is the most effective treatment with intensive auditory-verbal therapy. Prior to the advent of CIs, most patients were trained in sign language. Cochlear implantation has changed the course of intervention reducing the impact of hearing issues for the patient with Usher.

Treatment and Intervention Considerations

For individuals who have been diagnosed with Usher syndrome, connecting with an agency that can provide comprehensive Vision Rehabilitation Services will be critical to their overall adjustment and success in learning to live with the combined challenges of hearing and vision loss.

Treatment and Intervention Considerations

Certified Vision Rehabilitation Therapists and Orientation & Mobility Specialists provide training in new skills and strategies for learning to live with reduced vision. They can introduce tools and technologies that will maximize independence while simultaneously provide training that demonstrates to the individual that independence in all life activities is still possible.

Treatment and Intervention Considerations

This “guided success” approach is the key to successful adjustment and most organizations that provide this service are able to do so throughout the individual’s entire journey – providing training and support as the vision and/ or hearing continue to degrade over time.

Treatment and Intervention Considerations

Some ophthalmologists believe that a high dose of vitamin A palmitate may slow, but not halt, the progression of retinitis pigmentosa. This recommendation was based on the findings of a long-term clinical trial supported by the National Eye Institute and the Foundation for Fighting Blindness.

Treatment and Intervention Considerations

Researchers recommended that most adult patients with the common forms of RP take a daily supplement of 15,000 IU (international units) of vitamin A in the palmitate form under the supervision of their ophthalmologist. This vitamin therapy is still controversial, however.

Treatment and Intervention Considerations

Physical and/or occupational therapy can help ameliorate some of the issues associated with an impaired or absent vestibular system.

Poll Question 6

Treatment and Intervention Considerations: Case Study

- Twins, born at 32 weeks
- ABR in the hospital profound hearing loss AU
- Genetic testing: Connexin 26
- First Cochlear implant at 12 months
- Intensive Auditory training, began talking within six months of CI. Attained excellent listening and spoken language skills.

Treatment and Intervention Considerations: Case Study

- Second CI at 4.5 years, mainstreamed in private school by kindergarten
- Vestibular dysfunction noted early on, but discounted because they were premature
- Since they thought the etiology of hearing loss was Connexin, no one ever mentioned Usher
- At age 12, one twin started having difficulties with her night vision

Treatment and Intervention Considerations: Case Study

- Ophthalmologist saw yellow spots on her retina, Retinal specialist noted Rod Dystrophy
- Parents looked up on internet and found Usher Syndrome (though no one else had mentioned it)
- ERG and genetic testing confirmed Usher in both twins Type IC

Treatment and Intervention Considerations: Case Study

- Twins are now 14 years old, doing well in 8th grade at an academically challenging school.
- Early, bilateral cochlear implantation decreased the impact of the hearing loss.

Treatment and Intervention Considerations: Case Study

- For all my patients with Usher, early implantation has made a difference
- In hind sight, all had vestibular issues as babies and young children
- At this time, because of the CI, hearing loss is less of an issue than their vision loss

Research

NIDCD researchers, along with collaborators from New York and Israeli universities, pinpointed a mutation, named R245X, of the *PCDH15* gene that accounts for a large percentage of Type I Usher syndrome in the Ashkenazi Jewish population. The researchers recommended that Ashkenazi Jewish infants with bilateral, profound hearing loss who lack another known mutation that causes hearing loss should be screened for the R245X mutation.

Research

Scientists are working to identify and determine the function of all of the genes that cause Usher syndrome. This research will lead to improved genetic counseling and early diagnosis, and may eventually produce more treatment options.

Conclusion

Current Newborn Hearing Screenings and follow-up audiological testing only provide for recognition of hearing loss. Although genetic testing is sometimes recommended, even then, it is often limited to “hearing” genes; therefore, limiting the possibility that an Usher gene is detected.

Conclusion

Early treatment is recommended including hearing aids, assistive listening devices, cochlear implants; orientation and mobility training; and communication services and independent-living training that may include Braille instruction, low-vision services, speech-language therapy, auditory-verbal training.

Conclusion

Audiologists, otologists, auditory-verbal and speech-language therapists, and ophthalmologists should be aware of the characteristics associated with Usher Syndrome and recommend genetic testing that includes Usher genes, as well as a referral to a retinal specialist.

Special thanks to my co-contributors:

Melissa K Chaikof
Usher 1F Collaborative
Susan Trotochaud
Usher 2020 Foundation
Nancy Parkin-Bashizi
Vision Rehabilitation Services of Georgia

References

- http://www.sense.org.uk.content/usher-syndrome
- Kranowitz, Carol Stock. *The Out-of-Sync Child* (New York, NY: Berkley Publishing Company, 1998), 95-129.
- http://www.stichtingmus.nl/uploads/files/Vestibular_Poster_7-7-14_study_design.pdf
- First International Symposium on Usher Syndrome and Related Disorders, Boys Town National Research Hospital, Omaha, NE, October 3-6, 2006
- http://understandingwilliamssyndrome.blogspot.com/p/muscles-and-bones.html
- Cognitive Aspects of Vestibular Disorders, Kenneth Erickson, M.D., VEDA Conference, Portland, Oregon

Resources

- Usher 1F Collaborative: www.usher1f.org
- Usher 2020 Foundation: www.Usher2020.org
- Usher Syndrome Coalition: www.usher-syndrome.org
- Usher Syndrome - Fighting Blindness: www.fightingblindness.ie/eye-conditions/usher-syndrome

THANK YOU!