Identification and Management of Children with Usher Syndrome

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Abstract

Usher Syndrome is a rare genetic disorder that is the leading cause of deaf-blindness in the world. It was named for a Scottish Ophthalmologist from the early 1800s, Charles Usher, who recognized it as a syndrome through a number of his patients.

Although it is rare, only about 45,000 people in the U.S., it is devastating for those who are affected by it. Caused by an autosomal recessive gene, it manifests itself in three clinical types.

Early diagnosis is critical for children with Usher syndrome. While there is currently no cure, the best treatment involves early identification so that educational programs and assistive technologies can begin as soon as possible. Early, bilateral cochlear implantation is an effective treatment for children with severe to profound hearing loss.

Parents rely on audiologists for information and guidance in working with their children who have hearing loss, so the audiologist is often expected to counsel and help parents through their choices and decisions. The purpose of this paper is to educate educational programs and assistive technologies named for a Scottish Ophthalmologist from the early 1800s, Charles Usher, who recognized this syndrome as retinitis pigmentosa in which he recognized this syndrome as an inherited disorder. Usher’s work was a continuation of research on retinitis pigmentosa begun by Albrecht von Graefe and Richard Liebmann in the late 1850s.

Prevalence

Although Usher Syndrome is rare, with the incidence 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 hearing loss have Usher Syndrome and an estimated 50% of all people who are deaf and blind. It is believed that 3 to 6% of all children who are deaf have Usher Syndrome.

Clinical Features

Vision Loss

The gradual visual loss in people with Usher Syndrome is caused by Retinitis Pigmentosa or RP. In Usher Syndrome, RP is caused by a mutated gene in the retina that does not produce a protein needed by the rods to survive. 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. In Type I Usher, 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. The regression of RP can occur at different rates in different individuals, but many people with Usher Syndrome are legally blind by early adulthood.

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. 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.

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.

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. Type III Usher syndrome presents 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. This clinical type, while common in Finland, is extremely rare in the United States.

Vestibular Dysfunction

Usher Syndrome Type 1 (USH1) 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 USH1. The presence of vestibular dysfunction in a child with profound sensorineural hearing loss could suggest USH1. In fact, 36% of those born with profound deafness and vestibular dysfunction have USH1. As other sources of profound deafness with vestibular issues are ruled out, the likelihood rises.

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

Late sitting – Sitting between ages 9 and 12 months rather than by age 7 months. Tripod position until then.

Late crawling, often starting with a combat crawl

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

Preschool and Early Childhood:

Avoided, uncoordinated and clumsy at playground games

May fall often and easily

Bumping into furniture

Losing balance when pushed slightly off their center of gravity

Later Childhood through Adult:

Decreased ability to track two processes at once

Difficulty in handling sequences

Increased mental stamina

Memory retrieval ability

Decreased sense of internal certainty

Decreased ability to grasp the large whole concept

Genetic Features

Caused by an autosomal recessive gene, it manifests itself in three clinical types. 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 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. Type III includes progressive hearing loss, possible vestibular issues, and progressive vision loss through RP.

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

<table>
<thead>
<tr>
<th>Clinical Type</th>
<th>Gene Type</th>
<th>Human Gene</th>
<th>PhenoType</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>USH1, USH1C</td>
<td>MYO7A, USH1C</td>
<td>HEARING</td>
</tr>
<tr>
<td></td>
<td>Usher 1F Collaborative, Boston MA</td>
<td>USH1G, USH1H</td>
<td>Born with severe to profound hearing loss.</td>
</tr>
<tr>
<td>Type II</td>
<td>USH2A, USH2C</td>
<td>USH2A, USH2C</td>
<td>Born with mild to severe hearing loss with progressive loss into adulthood.</td>
</tr>
<tr>
<td>Type III</td>
<td>USH3A, USH3B</td>
<td>CLRN1, CLRN3</td>
<td>Born with normal hearing with progressive hearing loss developing in adolescence to early adulthood.</td>
</tr>
</tbody>
</table>

Treatment and Intervention Considerations

At present, 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. In Usher Type II and III, assisted hearing is recommended as soon as the hearing loss is identified by speech-language or auditory-verbal therapy. Most of these children will do well with early intervention. For Type I Ushers, early, bilateral cochlear implantation is the most effective 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 syndrome.

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. 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. 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.

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

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

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. 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. 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.

References


First International Symposium on Usher Syndrome and Related Disorders, Boys Town National Research Hospital, Omaha, NE, October 3-6, 2006

Cognitive Aspects of Vestibular Disorders, Kenneth Erickson, M.D., VEDA Conference, Portland, Oregon.