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Low Vision Rehabilitation Management for Retinitis Pigmentosa

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Abstract:

Retinitis pigmentosa is a group of inherited, progressive retinal dystrophies caused by mutations that lead to rod photoreceptor loss and subsequent cone photoreceptor loss. Common symptoms include nyctalopia, peripheral vision defects, and eventual central vision loss. Treatments include management of secondary findings such as cystoid macular edema and posterior subcapsular cataracts. Retinal prostheses and gene therapy have also proven to be promising treatments. In addition, low vision rehabilitation can help patients continue to maintain an independent lifestyle. This case reviews the rehabilitation management of a patient with an advanced level of retinitis pigmentosa.

Key words: retinitis pigmentosa, low vision rehabilitation, legal blindness, retinal prosthesis, gene therapy, orientation and mobility

Introduction

Retinitis pigmentosa (RP) is a set of inherited rod-cone degenerative diseases that clinically presents with similar signs and symptoms. Patients will commonly present with bone-spicule pigment formation, waxy optic nerve pallor, and attenuated blood vessels in the posterior pole. Symptoms often begin with progressive night blindness, mid-peripheral visual field defects, and eventual tunnel vision. Central vision loss will ultimately occur following loss of rod function. Central vision may also become impaired from secondary complications including posterior subcapsular cataracts and cystoid macular edema. There is currently no cure for RP, but some treatments include interventions for secondary complications, retinal prosthesis implants, and gene therapy.

RP is one of the most common causes of severe vision impairments[1] and can significantly affect daily life, impacting activities such as driving, reading, and mobility. Low vision rehabilitation services are available to improve visual function through devices, to assess safe mobility, and to connect patients with resources to maintain levels of independence.

Case Report

A 78-year-old African American female presented for a low vision consultation on March 15, 2018. She was referred by a local retinal ophthalmologist whom she saw two weeks prior for an initial comprehensive ocular health examination. The patient had recently moved from out-of-state approximately one month prior and was re-establishing care. The patient was legally blind secondary to retinitis pigmentosa, which was diagnosed in her 50s. The patient reported gradually progressive hazy central vision and decreasing peripheral vision in both eyes. She reported severe night blindness and restricted her travel at night. She also felt colors were becoming more difficult to distinguish and needed higher contrast materials to read.

Other than the diagnosis of retinitis pigmentosa in both eyes, the patient had no other remarkable ocular conditions. She reported having cataract surgery and yttrium aluminum garnet (YAG) capsulotomy in both eyes over 10 years ago. She reported a diagnosis of hypertension, which was controlled with atenolol, and recent gastrointestinal issues including nausea and diarrhea. She reported taking gabapentin for unknown nerve pain and simvastatin for high cholesterol. She had no known drug allergies. Her family medical and ocular histories were non-contributory. She denied any family history of retinitis pigmentosa. She was a social drinker and had never smoked.

The patient was dilated and examined two weeks prior on March 2, 2018, by a retinal specialist. Findings at that visit included unaided distance visual acuities of counting fingers at two feet in both eyes. Pupils were round with brisk responses. Extraocular muscle motility was full in both eyes. Confrontation visual fields were noted as temporal loss in the right eye and superior and temporal loss in the left eye. She had normal ocular adnexa and quiet lids, conjunctiva, and sclera in both eyes. Corneas in both eyes were noted as clear epithelium, clear stroma, and clear endothelium. Anterior chambers had normal depth and were quiet. Iris was flat in both eyes. She had centered posterior chamber intraocular lenses in both eyes. Intraocular pressures were noted as 12mmHg in both eyes with Tonopen. The patient was dilated with 1% tropicamide and 2.5%

phenylephrine with 0.5% proparacaine instilled in both eyes. The vitreous was clear in both eyes. Both optic nerves were measured as 0.4 cup-to-disc ratios with no disc edema, disc hemorrhages, notching, or thinning noted. Waxy disc pallor and attenuated blood vessels were observed in both eyes. The macula in both eyes had retinal pigment epithelium (RPE) changes with no edema or hemorrhages. Bone spicule changes were noted 360 in the periphery of both eyes with no holes or tears (Figure 1). An optical coherence tomography (OCT) scan showed RPE changes and no evidence of macular edema or subretinal fluid in both eyes(Figure 2). The patient reported a history of ancillary testing in her 50s when she was diagnosed with retinitis pigmentosa. She did not recall the name of the test or doctor who performed the test. From her description, an electroretinogram (ERG) was most likely performed, which she reported resulted in positive findings for retinitis pigmentosa.

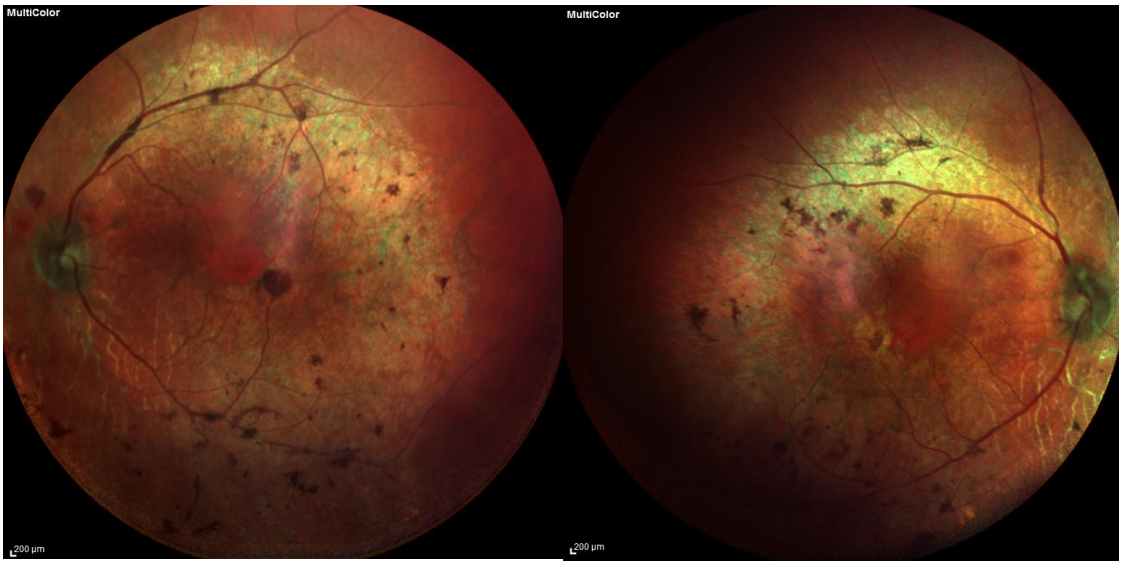

Figure 1. Posterior pole fundus photographs of the left eye (left) and right eye (right): waxy disc pallor, attenuated vessels, RPE changes in macula, and bone spicule changes noted in both eyes.

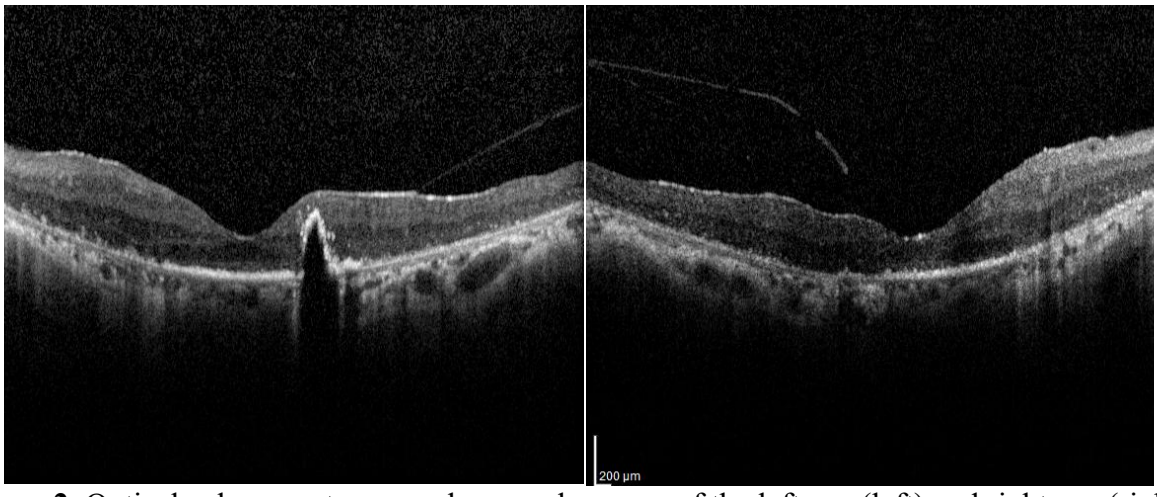

Figure 2. Optical coherence tomography macular scans of the left eye (left) and right eye (right): signs of photoreceptor loss, RPE changes, and no intraretinal or subretinal fluid noted.

The patient's son accompanied her to the low vision consultation. He was temporarily living with her as she settled into her newly purchased home. She regarded herself as a very independent woman and reported living alone before moving. Her main goal for low vision rehabilitation was reading and a desire to be fit with a stronger reading prescription. She was currently using several different pairs of reading glasses, all of which she found unhelpful. She reported being an avid reader in the past and enjoyed reading novels and newspapers.

At the low vision examination, entering unaided distance visual acuities were 10/140 in the right eye and $10/140^{+}$ in the left eye measured with the Feinbloom chart. Near visual acuities with her preferred +6.50 diopter (D) readers were 2.5M in the right eye and 2M in the left eye measured with single letters at 15 centimeters (cm). The patient was allowed to hold the near chart at any distance to evaluate her preferred working distance. With both eyes open using the +6.50D readers, the patient read the 2M line with difficulty on the Mn Read continuous text reading chart at 15cm. The patient initially reported that she preferred using the +6.50D readers combined with a +4.00 clip-on for reading. However, when tested with this combination in office, the patient was unable to hold the material at the correct working distance and struggled to read the 4M line. A trial frame refraction did not result in an improvement in visual acuity in the right eye but did result in an objective and subjective improvement in the left eye to $10/120^{+}$ with +2.50 -1.50 x 075. Full-time wear of single vision distance glasses with polycarbonate lenses were recommended for improved clarity of vision and protection. A prescription for glasses was released to the patient.

Of the near devices evaluated, the patient most preferred the single vision prism readers. A 5x/16D illuminated hand-held magnifier (IHHM) and 4x/12D illuminated stand magnifier (ISM) were demonstrated to the patient with negative responses. The patient was unable to hold the IHHM stable at the correct focal length for full magnification and she regarded the field of view too small. Though the ISM had greater stability as the device rests directly on the page, she preferred using a hands-free option for reading. From her near acuities, a +13D effective add would, in theory, help her read the 1M line at 7.5cm. Due to her resistance in holding the reading material at a close working distance, a lower powered +8D prism reader was demonstrated. A stock prism reader instead of a trial frame was used in this demonstration for convenience and comfort for the patient. Proper, close working distance was discussed extensively with the patient. She was able to read the 1.6M line at 12cm with the +8D prism readers. Now that she understood the working distance concept, she desired to try a stronger pair of prism readers. She reported that she would be willing to compromise the working distance in order to read. A +12D pair was demonstrated to the patient with a positive response. She was able to read the 1.3M line at 8cm. She preferred the +12D prism readers and was not interested in evaluating stronger powers. She did not wish to hold the material any closer. The importance of proper, direct lighting with these strong reading glasses was discussed as well.

Contrast sensitivity was measured with the MARS chart to be 0.4 log units, indicating profound loss. Due to such severe contrast sensitivity loss, electronic video magnification with enhanced contrast settings was strongly recommended to the patient. She had a very positive response to the portable electronic video magnifying system Visolux HD from Eschenbach. She greatly appreciated the white on black setting and zoom functions. She preferred the larger screen of the Visolux HD compared to the smaller Ruby XL HD device. A Ruby 7 with a comparable 7-inch

screen size to the Visolux HD and distance camera capabilities was also shown to the patient. She did not appreciate the need for the distance camera function at this time and preferred the less costly Visolux HD device. The Topaz HD desktop video magnifier or closed-circuit television (CCTV) was also demonstrated to the patient as an option for a larger screen with similar contrast enhancement and zoom functions. She had a positive response to the device; however, due to her active lifestyle, she preferred the portable video magnifier for convenience.

Non-seeing to seeing confrontation visual fields with a transilluminator were restricted in both eyes. In the right eye, superotemporal and superonasal fields were restricted to five degrees, inferotemporal restricted to 45 degrees, and inferonasal restricted to 45 degrees with a mid-peripheral scotoma from 10 to 30 degrees. In the left eye, superotemporal and superonasal fields were also restricted to five degrees, inferotemporal restricted to 45 degrees, and inferonasal restricted to 60 degrees with a mid-peripheral scotoma from 10 to 30 degrees. It was observed that the patient often used slight superior eccentric viewing when talking with others, most likely due to her severely restricted superior fields. With such limited fields, the patient was questioned further about her mobility issues. The patient's son reported the patient having frequent stumbles and bumping into objects she did not see. The patient reported no falls and exercised extreme caution when walking in unfamiliar areas. She ambulated cautiously without a cane or walker. Orientation and mobility training was discussed and strongly advised to the patient for safe navigation. The patient was receptive to the recommendation as she was aware of her limitations due to reduced peripheral and central vision.

Low vision services are able to connect patients to resources for other aspects of their lives impacted by vision loss. Since the patient was not a driver, alternative transportation options were reviewed. The patient desired to be independent and transportation was an issue. In many cities, there are transportation alternatives provided to those with disabilities. Many of these applications require doctor prescriptions or verifications of visual impairments and optometrists are able to help provide this documentation. A shared-ride public transit service in the city that provided free transportation services for individuals with visual impairment was discussed. An application was completed and released to the patient. Another subsidized program that offered transportation at a 50% discounted price and allowed for same-day scheduling was recommended as well. This application was released to the patient. A disability placard application was offered to the patient, but the son reported that they already had one in place. Helping patients find alternative transportation is important, as transportation is a crucial aspect for independent living.

Pupils were equal, round, and reactive to light in both eyes with no afferent pupillary defects. Extraocular muscle function was full with no restrictions in either eye. Ocular adnexae, lids, lashes, and conjunctiva were unremarkable in both eyes. Corneal incision scars from past cataract surgery and well-centered posterior chamber intraocular lenses were noted in both eyes. The anterior chamber was deep and quiet in both eyes. A small pupil 90D lens fundus examination was attempted but views were limited due to miotic pupils. Since the vision was stable and the patient did not report any visual changes since her last dilated examination two weeks prior, dilation was not performed at this visit.

In summary, the patient was legally blind secondary to retinitis pigmentosa in both eyes. Her Snellen equivalent visual acuities were 20/400 in the right and left eyes, which qualified her for legal blindness status. A letter of legal blindness was released to the patient. Due to financial difficulties, an application for the Independent Living Services for Older Individuals Who Are Blind (OIB) program was completed and sent to the State Workforce Commission (SWC) to open a case for her. The SWC is a state agency that provides support services for those with disabilities to obtain training and employment. The OIB program is a particular branch in SWC that allocates services and resources to patients 55 years and older with visual impairments to help them maintain an independent lifestyle. The OIB program is able to provide the patient with orientation and mobility training, low vision devices, and independent living skills training. An Eye Report and letter were sent to the SWC as an application for the OIB program with the patient's written authorization for release of medical records to SWC. Orientation and mobility training, single vision distance glasses with polycarbonate lenses for protection, and the +12 prism readers were requested through the OIB program. Once the application is accepted, the patient will return to the University's optical to choose a frame for the glasses and for a dispense of the prism readers. If she desired not to wait for the application process, she was given a copy of the single vision distance prescription to order glasses and the option of ordering devices through private pay. Private orientation and mobility instructors were also discussed, but financially difficult for the patient to pursue.

Discussion

Retinitis pigmentosa (RP) is a heterogeneous group of diseases that causes death to rod photoreceptors and subsequent loss of cone function in both eyes. There are more than 3,000 genetic mutations in approximately 70 known genes that are associated with RP.[2] These genes consist of those involved in phototransduction, photoreceptor structure, or gene transcription in photoreceptors.[3] Depending on the mutation, rod cell death may degenerate at different rates and levels of severity. This condition can present as an autosomal dominant, autosomal recessive, X-linked, or unknown pattern inheritance. Unknown pattern inheritance with no family history of RP is the most common at 40-50%, as the patient in this case.[2] Mode of inheritance is important as it may determine the prognosis and severity of the disease. A male with X-linked RP has the worse prognosis, resulting in a visual acuity of 20/200 or worse in almost all patients over 50 years old.[4] Autosomal recessive inheritance has an intermediate prognosis and autosomal dominant has the best prognosis.[4] However, each individual patient's prognosis can vary greatly as there are many mutations within each mode of inheritance making the molecular genetics of RP complex. The prevalence has been estimated to be 1:4000[1,5] or a range between 1:750 to 9000.[6] Approximately 2.5 million people worldwide are affected by RP.[2] There was no significant gender predilection found in literature. RP may present alone (nonsyndromic) or with other systemic effects (syndromic). Syndromic RP is less common at 17% of RP cases.[4] Of the syndromic RP conditions, Usher syndrome is the most common with manifestations of hearing defects.

The pathophysiology of RP begins with rod photoreceptor degeneration and leads to cone photoreceptor degeneration as well. Mutations can occur in many processes involving the rod photoreceptors, ranging from rod visual transduction to metabolism and RNA processing.[7] Mutations can also cause rod photoreceptor defects in rhodopsin processing and trafficking,

defects in rhodopsin stacking, and deficiencies in cilia function.[8] These mutations directly affect the function of rod photoreceptors; however, they do not directly affect cone photoreceptors. Cones only become affected after almost all of the rods are lost.[4] Hence, the longer the rods survive, the better the prognosis for cone function. One theory of the mechanism for eventual cone death is the level of oxidative damage after rod degeneration.[4] As the rods atrophy, the level of oxygen in the retina increases due to the lack of oxygen consumption by viable rod photoreceptors. With higher oxygen levels, the incidence of free radicals, superoxide radical production, and peroxynitrite-induced damage increases, causing damage to cones.[4]

There are many characteristic symptoms patients with RP experience. Patients with RP initially present with nyctalopia as rod photoreceptors primarily involve vision in dim illumination. Symptoms are initially noticed in dim light settings and commonly begin during adolescence.[2] Onset of night blindness that occurs at an earlier age usually indicates a worse prognosis and more rapid progression of visual function loss.[4] The next symptom is often constriction of visual fields, particularly in the mid-periphery, where the cone receptor density is low.[4] The field defects coalesce into a mid-peripheral ring scotoma that progresses peripherally and centrally, ultimately leaving a central island of vision. Islands of peripheral vision may remain due to clumps of viable cones that have migrated together.[9] In advanced disease, patient will have central vision loss in daylight as the cones degenerate further. Eventually, all photoreceptors will be lost, leading to complete blindness. Fortunately, complete blindness was found to be rare in past studies.[1011] However, most patients with RP are classified as legally blind (20/200 or worse in the better seeing eye or 20 degrees field or less in the better seeing eye) by the age of 40.[12]

The classic triad found in RP includes bone spicule pigment, attenuated blood vessels, and waxy pallor of the optic nerves. The formation of bone spicule pigment is thought to be due to the proximity of retinal blood vessels to the RPE, triggering the migration of RPE cells.[1] The loss of the photoreceptor layer reduces the retinal thickness, allowing contact of the RPE cells to the blood vessels, and initiating the migratory behavior of RPE cells. These clusters of RPE cells eventually surround the blood vessel capillaries and form the bone spicule pattern.[1] As rod photoreceptors degenerate, oxygen levels increase in the outer retinal layers and spill over into the inner layers. This increase in oxygen causes the blood vessels to constrict and appear attenuated in order to maintain normal retinal oxygen tension.[4] In RP, optic nerve pallor does not indicate optic atrophy and is not considered to be the cause for vision loss.[13] One common cause of vision loss is cystoid macular edema (CME). A combination of various etiologies may contribute to the onset of CME including breakdown of blood-retinal barrier, dysfunction of RPE pumps, Muller cell dysfunction, and vitreous traction.[14] An estimated range of 10-50% of patients with RP develop signs of CME.[1415] Another common cause of reduced central vision is posterior subcapsular cataracts. Approximately 41-53% of patients with RP had signs of PSC, according to previous studies.[16] Though the mechanism for PSC development in RP is not clear, it has been shown that elevated aqueous flare is a risk factor for PSC formation, indicating an inflammatory process.[16]

Diagnosis of RP is often based upon characteristic appearances, but ancillary testing can also be performed. A full-field or multifocal electroretinogram (ERG) is often performed to confirm diagnosis. The scotopic a- and b-wave amplitudes measuring mainly rod function are reduced in all types of RP and photopic (cone) b-wave amplitudes are gradually reduced as well. A full-field

ERG measures responses from the entire retina while a multifocal ERG is able to stimulate the central macular region alone. Multifocal ERG is more advantageous to use in following advanced RP cases for visual function.[17] OCT is another critical test to perform for patients with RP to confirm the absence of CME, especially if visual acuity is reduced. Humphrey visual field testing can also help monitor the progression of visual field defects in RP and is a way to follow the progression of the disease. Visual field testing can also qualify patients for legal blindness status (20 degrees diameter visual field or less in the better eye tested with a sizeIII4e target).

Some differential diagnoses for retinal degenerations include:

- Gyrate Atrophy
- Choroideremia,
- Cone-rod dystrophy
- Leber's congenital amaurosis

- Gyrate atrophy presents with a different appearance of large, pavingstone-like lesions in the periphery from RPE and choriocapillaris atrophy. In advanced forms of gyrate atrophy, these lobular lesions coalesce to form a scalloped border in the mid-periphery

- Choroideremia can also be differentiated by retinal appearance. Initially, choroideremia presents with pigment formation throughout the fundus; however, the pigment clumping is at the RPE layer rather than perivascular bone spicule clumping as in RP.[18] RPE, photoreceptors, and choriocapillaris eventually atrophy leaving visible underlying sclera and larger choroidal vessels.

- Cone-rod dystrophy may have similar fundus appearance; however, central visual acuity and color vision are normally affected before loss of peripheral vision or onset of nyctalopia.[17]

- Leber's congenital amaurosis (LCA) onset is earlier and the prognosis more severe than RP. Patients with LCA typically have severe vision loss by one year of age and present with nystagmus, poorly reactive pupils, and oculo-digital sign.[17]

The wide cast of mutations that cause RP makes treatment challenging. Pharmacologic therapies have not proven to be clinically significant. These agents include neurotrophic, antioxidant, anti-apototic, and anti-inflammatory. Vitamin A has been a controversial therapy and may cause potential adverse effects. Further studies need to be completed to confirm clinical efficacy of pharmacologic therapies. For secondary complications of CME, carbonic anhydrase inhibitors (CAI) have been shown to be the most effective therapy and the main line treatment for CME secondary to RP.[2] A proposed mechanism of CAI for CME from RP includes promoting fluid resorption by restoring normal carbonic anhydrase activity along the basolateral membrane of RPE cells by blocking different anhydrase isozymes. It has also been shown that CAIs enhance blood flow and oxygen tension on retinal vasculature, increasing fluid resorption. There were less systemic side effects from topical CAI compared to oral CAI.[15] Another secondary complication of posterior subcapsular cataracts is treated by cataract surgery, as the patient above had been previously.

Retinal prosthesis is a promising treatment for end-stage cases of RP. Retinal prostheses utilize remaining functional inner retinal cells to induce neural activity. As RP progresses, photoreceptors lose function, but ganglion cells remain functional.[19] Retinal prostheses circumvent the absent photoreceptors by converting light information into electrical signals and stimulating neurons downstream in the visual pathway. The Argus II Retinal Prosthesis System is an epiretinal prosthesis that has been approved by the U.S. Food and Drug Administration (FDA) and is the first to be commercially available for patients. The system utilizes a small camera mounted on a pair of glasses connected to a video-processing unit that collects, processes, and sends signals to a receiving antenna implanted in the eye. Patients perceive these signals as patterns of light.[20] Currently, the inclusion criteria is visual acuity of bare light perception or worse in both eyes due to profound RP.[12] Improved basic visual function include target localization, direction of motion, mobility, and orientation.[2,20]

Gene therapy for retinal degenerations has been an area of great research. LUXTURNA, voretigene neparvovec (AAV2-hRPE65v2), is the first U.S. FDA-approved gene therapy for RPE65-mediated retinal dystrophy. Positive outcomes have included improved light sensitivity, visual fields, and mobility in dim lighting.[21] It carries an adeno-associated virus vector containing the human RPE65 complementary DNA that is injected subretinally. Inclusion criteria consist of patients with visual acuity 20/60 or worse or visual field less than 20 degrees.[21] Patients also need a confirmed genetic diagnosis of biallelic RPE65 gene mutations as the cause of RP.[21] Unfortunately, RP associated with RPE65 mutation has been found to be rare, approximately 2% of autosomal recessive RP.[22] The patient in this case was not interested in genetic testing and preferred to use low vision devices and compensatory strategies to function at this time.

Low vision rehabilitation services are crucial for patients in all stages of RP. In early stages, proper education about the disease symptoms and prognosis is critical. As the condition progresses, it is imperative to monitor for visual field defects. Visual field is a strong predictor for poor mobility function.[23] Without independent mobility, a patient's quality of life suffers. It is recommended that patients with visual fields less than 70 degrees be evaluated carefully for mobility issues and consider orientation and mobility (O&M) training.[23] Patients with 31 to 52 degrees fields have even higher risk for mobility difficulties and a restriction to 15 degrees should have immediate referral for mobility rehabilitation.[23] Furthermore, if there is central vision loss in addition to peripheral restriction, referral for assessment should be considered even earlier as is the case for this patient. O&M training is designed to help patients navigate safely and independently in familiar and unfamiliar environments. O&M specialists can help patients utilize remaining functional vision with their other senses and can also teach efficient white cane travel. Prompt referral for mobility rehabilitation is necessary due to its limited resources and the significance of independent travel for quality of life. Alternative transportation options should also be discussed, as patients may not have sufficient visual fields or visual acuities to meet recommendations for a driver's license. As central vision becomes involved, low vision magnification devices such as high-powered readers, illuminated hand-held, and stand magnifiers may benefit the patient. Video magnifying systems (VMS) with its enhanced contrast features may especially assist the patient as contrast sensitivity becomes greatly reduced. Profound loss of vision may indicate for audio devices such as the OrCam reader or CCTVs with optical character recognition. Distance magnification includes monocular telescopes, binocular spectacles, electronic devices, and more. Success of magnification devices will vary depending

on the level of RP and subjective preference. It is beneficial to demonstrate various devices of differing functionalities in order for patients to gain an understanding of the many options available to them. Keeping patients independent with low vision rehabilitation helps maintain confidence levels, emotional health, and satisfaction with life.[24]

Conclusion

Retinitis pigmentosa is a serious, degenerative retinal condition that has substantial benefits from low vision rehabilitation services. Beyond device magnification, an essential consideration for rehabilitation is orientation and mobility training for safe navigation. Vision-related functions such as mobility need to be questioned and addressed as patients may not initially offer this information or recognize the issue. Continual research is being performed to find treatments to halt or slow progression of photoreceptor degeneration or introduce means of bypassing the diseased retinal layer. Optometrists should be up-to-date with current research and be familiar with newly approved therapies.

A low vision consultation is often the beginning of a road to long-term rehabilitation with RP as it is a progressive condition. The first visit is a stepping-stone for patients to continue this uphill journey. The patient in this report left the clinic hopeful and confident in the potential of maintaining independence. Low visions services not only provide evaluation of devices for improved vision, they also are able to introduce various available resources to patients. Low vision specialists have a unique place as strong advocates for patients. Overall, low vision rehabilitation manages the patient holistically, addressing all areas of impact from this progressive retinal condition, and helping patients maintain a full and independent lifestyle.

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