Article • A Case Report of Familial Congenital Aniridia and Oculocutaneous Albinism with an Emphasis on Multifaceted and Multidisciplinary Patient Management

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ABSTRACT

Background: Congenital aniridia and oculocutaneous albinism impair ocular development and frequently present with overlapping signs and symptoms. Similar manifestations include foveal hypoplasia, optic nerve hypoplasia, iris abnormalities, congenital nystagmus, strabismus, and decreased visual acuity, which hinder quality of life in affected individuals.

Case Report: We present a case of a six-year-old male with both familial congenital aniridia and oculocutaneous albinism yielding secondary visual impairment. His low vision optometric care included refractive error correction, photophobia control, low vision device evaluation, strabismus and amblyopia treatment, ocular health examination and management, and functional vision assessment. The patient's specialty care team included a low vision optometrist, a pediatric glaucoma specialist, a strabismus specialist, a teacher of the visually impaired, an orientation and mobility specialist, and an occupational therapist.

Conclusions: The unique contributions of each member of the care team facilitate the holistic development of pediatric low vision patients. Appropriate management, including a multifaceted and multidisciplinary approach to care, is critical to maximize quality of life and visual potential.

Keywords: congenital aniridia, oculocutaneous albinism, pediatric low vision, pediatric optometry

Introduction

Congenital aniridia is a bilateral, panocular developmental disorder caused by an autosomal dominant mutation of PAX6, a critical gene that drives proper ocular development and plays a vital role in various other developmental processes. Numerous manifestations of the disorder present at birth, while others appear as later complications. Congenital aniridia encompasses a large spectrum of phenotypic variance, ranging from iris transillumination defects alone to near complete absence of the iris on gonioscopy.[1] Major associated ocular findings include congenital cataracts, foveal hypoplasia, optic nerve hypoplasia, congenital nystagmus, glaucoma, keratopathy, refractive error, and strabismus.[1,2] Individuals with congenital aniridia typically have a visual acuity ranging from 20/100 to 20/200 due to foveal hypoplasia.[1] Moreover, quality of life for these patients is further impacted by photophobia and impaired cosmesis resulting from the absence of iris tissue.

While often an inherited disorder, approximately one-third of congenital aniridia cases arise from a de novo mutation. When instances of sporadically acquired congenital aniridia involve the Wilms' tumor predisposition gene, the manifestations constitute WAGR syndrome. In addition to Wilms' tumor and aniridia, WAGR syndrome also involves genitourinary

abnormalities and intellectual delay.[2] The incidence of congenital aniridia reportedly falls between 1 in 64,000 and 1 in 96,000.[2] Glaucoma associated with congenital aniridia does not present at birth but rather develops later in childhood or adulthood. Similarly, the associated keratopathy typically has a delayed presentation, beginning at around age thirty as peripheral opacification and vascularization due to limbal stem cell deficiency.[3] This progresses over time and may be triggered by intraocular surgery.[4]

Oculocutaneous albinism (OCA) is a group of rare, autosomal recessive genetic disorders arising from mutations in melanin biosynthesis. Deficient melanin production leads to skin, hair, and ocular hypopigmentation.[5,6] Like congenital aniridia, significant phenotypic and genotypic variation exists within OCA. The two genetic disorders have many overlapping signs and symptoms, with both conditions often manifesting foveal hypoplasia, optic nerve hypoplasia, congenital nystagmus, refractive error, strabismus, reduced visual acuity, and photophobia.[5] A clinical distinction between the two developmental disorders is the state of the iris tissue. While aniridia is defined by an absence of iris tissue, OCA often exhibits a hypopigmented light blue or pink iris with transillumination defects.[5] Pathognomonic for OCA, increased fiber decussation at the optic chiasm as demonstrated by visual evoked potential studies leads to significant organizational changes in the visual cortex, with each hemisphere comprising mostly contralateral input.[6,7] This fiber maldevelopment impedes stereoacuity and binocular vision and can cause strabismus in these patients.[5,7] The various ocular, systemic, and functional manifestations of these two developmental disorders necessitate multifactorial and multidisciplinary care and collaboration for the patient's best life-long outcome.

Case Presentation

A six-year-old boy presented to the low vision clinic at the Perkins School for the Blind with his mother for a clinical functional low vision examination and formal visual field assessment.

The patient had been followed at the clinic for two and a half years. He had a history of congenital aniridia and oculocutaneous albinism with secondary foveal hypoplasia, congenital nystagmus, congenital cataracts, and left esotropia, for which he underwent strabismus surgery at age three. The patient's mother and maternal grandmother had a history of congenital aniridia with foveal hypoplasia, congenital nystagmus, and congenital cataracts. The patient's maternal grandmother developed secondary glaucoma and was subsequently monocular with an ocular prosthesis. Though there was an absence of confirmatory genetic testing, it was strongly speculated that the patient inherited both oculocutaneous albinism and aniridia based on the patient's clinical features and family history. The patient had no siblings. He was followed by a pediatric glaucoma specialist and a strabismus specialist. Ocular hypertensive medications had been prescribed by the patient's pediatric glaucoma specialist in the past for elevated intraocular pressures (IOP), but their use was discontinued per his ophthalmologist's instruction. His full-term birth followed an uncomplicated pregnancy. The remainder of the patient's medical history and review of systems was non-contributory.

The patient was wearing transition lens spectacles full-time to correct his bilateral hyperopia with astigmatism, and he owned polarized prescription sunglasses for outdoor wear. He had a history of yoked prism use for congenital nystagmus. He also had a history of left esotropia and associated strabismic amblyopia with a history of acuity improvement with patching treatment. He was patching his right eye for two hours daily, five days per week. The patient was receiving specialized services from a teacher of the visually impaired (TVI), an orientation and mobility specialist (O&M), and an occupational therapist (OT). He was also granted school accommodations through an Individualized Education Plan. At the current encounter, the patient's mother shared concerns regarding his reading and mobility. She also confirmed that his previously reported left head turn was still present but had lessened recently.

The patient's entering distance visual acuity (DVA) with correction (cc) using the M&S electronic acuity chart, single line, was 20/200 using both eyes, and the findings were similar with each eye individually. Near visual acuity (NVA) cc with the Lighthouse Near Card was 0.4m/3.2M (20/160) with both eyes, 0.4m/2.5M (20/125) with the right eye, and 0.4m/3.2M (20/160) with the left eye. The same evaluation with a paper-weight dome magnifier (enlargement ratio (ER): 1.6x) revealed an acuity of 0.1m/0.8M (20/160). Pelli-Robson contrast sensitivity cc was normal for age at 1.65 log units with both eyes together and with each eye individually. A minimal residual non-accommodative left esotropia at distance and near cc was observed, which was stable to previous examinations following strabismus surgery. The patient had a pendular

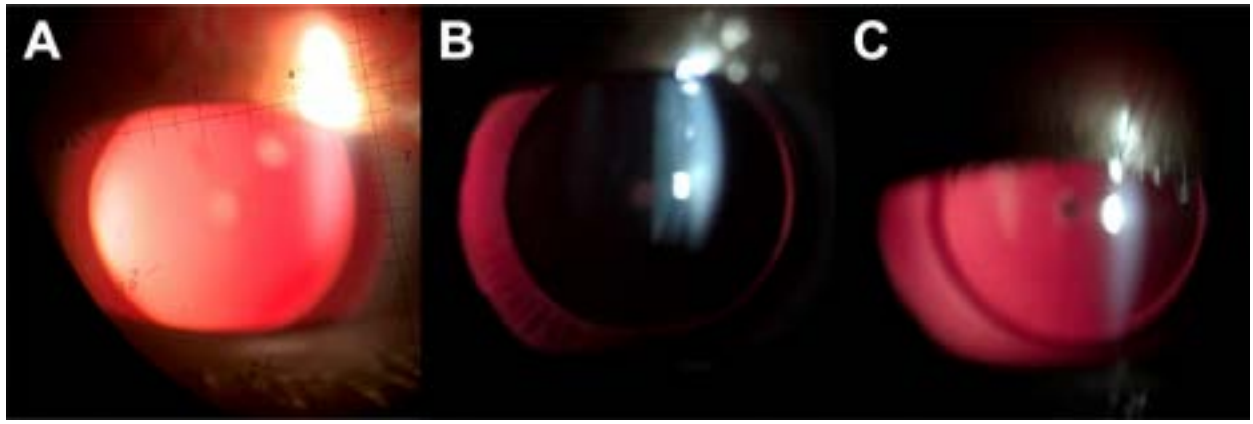

Figure 1. Slit lamp photos of the patient's anterior segment demonstrating (A) aniridia with retroillumination, (B) visualization of the zonules, and (C) a small anterior cataract with retroillumination

nystagmus with a null point in right gaze and full and extensive extraocular muscle movement in both eyes. He also continued to demonstrate a known red/green color vision deficiency. The patient's current spectacles measured OD: +5.00-0.50x005 and OS: +5.25-1.00x170, and dry over-retinoscopy was +1.00 sphere in each eye. Placing +1.00 lenses over the patient's current spectacle prescription provided no improvement in either the esotropia or the DVA. The patient showed nil gross stereoacuity cc on the Preschool Assessment of Stereopsis with a Smile test. Worth 4-dot testing, like previous examinations, yielded unreliable results.

Goldmann perimetry revealed full visual fields with both eyes and with each eye individually. Slit lamp examination demonstrated profound aniridia bilaterally (Figure 1), a small anterior cataract bilaterally (Figure 1), and clear, healthy corneas without keratopathy. His cataracts appeared stable to prior examinations. IOP using the iCare tonometer was 25 mm Hg in the right eye and 24 mm Hg in the left eye, an increase of 4 mg Hg and 1 mm Hg, respectively, from the patient's ophthalmology visit two months previously. Recent pachymetry findings were 703 µm of the right eye and 686 µm of the left eye. Internal ocular health revealed small optic nerves with a 0.20 cup-to-disc ratio and healthy rim tissue, foveal hypoplasia, and blonde fundi.

Low vision devices currently used by the patient included a white cane while at school, a closed-circuit television video (CCTV) magnifier, enlarged-print books, Humanware MATT connect tablet CCTV system, and a paper-weight dome magnifier (ER = 1.6x). He also used a laptop with magnification ability and an iPad with activated accessibility features. The patient was recently dispensed a Ruby handheld CCTV for home use to complete his homework and for pleasure reading. The clinical low vision evaluation incorporated a functional vision assessment that was shared with the patient's care team, including the TVI, O&M, OT, and ophthalmologists. The patient was registered with the Massachusetts Commission for the Blind, through which he received some of these specialized services.

Discussion

This case report of familial congenital aniridia and oculocutaneous albinism illustrates the disorder's impact on functional vision and quality of life while emphasizing the significance of specialized care in the management of these patients. Vision impairment throughout development, especially to the level of legal blindness, can remarkably impact quality of life by affecting occupational opportunities, education, social interaction, and qualification for a driver's license. Maximizing functional vision of pediatric low vision patients through a multifaceted and multidisciplinary approach to care will maximize quality of life. The multifaceted optometric low vision approach to care includes appropriate spectacle prescription, tinted lens evaluation, functional vision assessment, low vision device evaluation, strabismus and amblyopia management, ocular health assessment and treatment, and thorough patient and parent education. Optometric care is one component of the broader scope of multidisciplinary care that this patient receives for comprehensive management of his genetic ocular conditions. Other members of the comprehensive care team perform ocular surgeries, co-manage ocular disease, implement educational accommodations, assist with low vision device adaptation, employ home adaptations, and provide instruction for safe and independent travel.

The quantitative and qualitative results of our evaluation were shared with the patient's care team for integration into his multidisciplinary treatment plan. Some aspects of the clinical functional low vision

evaluation include assessment of visual acuity, contrast sensitivity, stereoacuity, color vision, ocular alignment, visual fields, low vision devices, and ocular health. The assessment thoroughly evaluates this patient's ability to interact visually with his environment. The patient's TVI uses this information to gain a better understanding of his functional vision in order to assist him effectively in the classroom by adapting learning to his abilities. Our assessment is useful to the O&M specialist so that she may provide instruction on safe and effective mobility techniques given the patient's DVA, visual field, contrast sensitivity, and stereoacuity. The occupational therapist works to acclimate the patient to his low vision devices and uses resources to foster independence and function in activities of daily living. The patient's ophthalmologists are provided with reports of the low vision examinations, allowing for comanagement and continuity of care. Likewise, these specialists provide information from their evaluations and interactions to the low vision optometrist.

The patient's reading performance did not improve with a dome magnifier of ER=1.6x at the current visit, but head position, unstable fixation secondary to nystagmus, and lighting likely all influenced acuity. He appreciated a subjective improvement, so he could continue using it for spot reading. The patient was dispensed a Ruby handheld CCTV for longer reading tasks like homework and pleasure reading. Yoked prism can correct anomalous head positioning associated with one's null point.[8] The effect of yoked prism on the patient's visual acuity will be revisited at future examinations. Low vision devices that improve reading comfort and efficiency are critical for the academic success of this first-grade patient who is learning to read. In addition to magnification devices, his young age allows for accommodative function at a short working distance; therefore, he has the ability to utilize relative distance magnification along with his other tools. The patient's photophobia has been successfully managed with transition spectacle lenses, polarized sunglasses, and a ball cap. Low vision device assessment and photophobia management will continue to be critical points of assessment at the patient's future functional low vision evaluations. He will continue patching his right eye as his fluctuating DVA had previously been greater with his right eye and his left eye's DVA previously improved with patching.". Augmenting visual acuity potential through amblyopia treatment is important for this young patient within the critical period of development.

Although the patient was only six years old, we considered his potential for obtaining a bioptic driver's license in the future. With his current DVA, he does not meet the Massachusetts vision standards for driving. However, his distance best-corrected DVA has fluctuated over the past two and a half years from near 20/100 in each eye to 20/200- in each eye, his most recent findings. This inconsistency is likely attributable to variable room lighting over multiple examinations and head position altering the effect of his nystagmus. Massachusetts' bioptic driving laws require a DVA in each eye of at least 20/100 through the carrier lens and 20/40 through the telescopic lens. Depending on forthcoming examination findings, a bioptic telescope assessment may be warranted when the patient is closer to driving age.

While many ocular findings of aniridia and OCA are non-progressive, a critical facet of care for these patients includes evaluating for multiple, progressive associated ocular diseases and systemic findings. The patient's family history of congenital aniridia significantly decreased our concern for Wilms' tumor in the context of a de novo PAX6 mutation, the cause of WAGR syndrome. Though ocular surgeries such as cataract extraction and iris prosthesis placement may alleviate some ocular manifestations of congenital aniridia, evidence suggests that surgical procedures in this population are associated with higher rates of complications to which they are already predisposed, particularly keratopathy.[4,9,10] Our patient's cataracts were not visually significant at this time, but cataract surgery may be indicated for him in the future. At that time, the risks and benefits should be carefully considered to determine whether the risk to functional vision is worth the benefit.

Unlike congenital glaucoma, which presents at birth, glaucoma associated with congenital aniridia develops later in childhood or adulthood, most commonly before the fifth decade of life.[11] Optometric low vision exams include measurement of IOP as part of the ocular health assessment to monitor for the development of glaucoma. Our patient's IOP typically measured in the ocular hypertensive range of 21-27 mm Hg. However, his thickened central cornea falsely elevates tonometry results. The patient's visual fields were reassuringly full in both eyes, and his optic nerves were healthy. Despite these reassuring factors, the patient should maintain frequent follow-up with his pediatric glaucoma specialist. Since the patient's mother and grandmother had a remarkably similar presentation and presumably the same causal

mutation, an observation of the familial phenotypic course of disease may provide valuable insight regarding our patient's susceptibility and risk of acquiring glaucoma.

Congenital aniridia and oculocutaneous albinism are complex genetic disorders presenting with overlapping panocular findings that create challenges for patients and hinder quality of life. This case of pediatric vision impairment demonstrates the value of optimizing functional vision through spectacle prescription, photophobia management, low vision devices, strabismus and amblyopia treatment, and routine ocular disease screening. Comprehensive treatment may enable patients to achieve important life milestones successfully, such as acquiring a driver's license and obtaining a meaningful education. A thorough family history in cases of aniridia is essential in order to investigate the possibility of systemic involvement. Comanaging in a multi-provider fashion with specialists including a low vision optometrist, pediatric glaucoma specialist, strabismus specialist, TVI, O&M, OT, nephrologist if indicated, and genetic counselor is critical to maximizing the care of patients with these developmental disorders.

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